ACTION OF MEDICINES.

THE

ACTION OF MEDICINES.

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WITH

TWENTY-TWO ILLUSTRATIONS.

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UND das Gefühl, welches der Physiologie empfindet wenn er aus einer unheimlich aussehenden mit Blut und zerstörtem Gewebe gefüllten Wunde irgend einen feinen Nervenzweig hervorholt und durch Erregung eine Function ins Leben ruft, die schon erloschen war; dieses Empfindung hat Vieles mit derjenigen gemein, welche den Bildhauer beseelt wenn er aus einer ungeformten Marmormasse schöne lebendige Formen herausbildet.— E. CYON.

TO

H. C. WOOD, JR., M.D.,

PROFESSOR OF THERAPEUTICS AND DISEASES OF THE NERVOUS
SYSTEM IN THE UNIVERSITY OF PENNSYLVANIA, IN
ADMIRATION OF HIS GREAT TALENTS
AND LABORS IN PHYSIOLOGI-
CAL THERAPEUTICS,

I Dedicate

THIS SMALL VOLUME.

PREFACE.

THE daily increasing interest in a knowledge of the physiological action of medicines is my motive in the publication of this book. The first volume on the physiological action of remedies was by Professor Nothnagel, followed by Professors H. C. Wood, Jr., Köhler, Hermann, and Brunton. The success of these works shows that the profession are seeking a more scientific basis in the explanation of therapeutic action. The study of the action of medicines has a threefold object: 1st. The advancement of Physiology; 2d. The explanation of a therapeutic action; 3d. The science of Toxicology in the discovery of antidotes, etc. To my mind the study of the action of a drug on the lower animals is the best practical training in science that a medical man can have. It gives to him a logical precision that will be most beneficial in his whole therapeutic life. He will not be apt to decide that because a certain result has followed the use of condurango that it is a valuable therapeutic agent or a specific. In this study he must perforce be made acquainted with the most important physiological functions.

The simplification of the labor of the student in the understanding of the action of medicines on the heart and nerves is also a much-desired object.

Whilst engaged in teaching and experimenting, a text-book that would give some idea how to investigate the action of drugs was found to be greatly needed. If this book meets the just-mentioned aims, the object of the author is fulfilled.

In giving examples of the action of atropia I have availed myself freely of the writers on the subject. The wood-cuts of instruments are from drawings of those given by the inventor or modified from the atlas of Cyon.

EASTON, PENNSYLVANIA,

December 1st, 1877.

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CHAPTER I.

HOW TO STUDY THE PHYSIOLOGICAL ACTION OF MEDICINES.

IN studying the action of drugs on lower animals the first requisite is a good practical knowledge of physiology. No "paper physiologist" will be able to make any observations and experiments on which any great reliance can be placed. For the necessary training, work in a physiological laboratory should precede the study of the action of medicines. In the absence of any accessible laboratory, private laboratories must be furnished and aid sought from handbooks in the acquirement of physiological facts. It is highly important to know the physiological function of an organ before the action of a drug on the same is studied. Experiments must be often repeated, for the same procedure often gives varied results, owing to the manifold changes in organic life. Where metamorphosis is constant, the ability to weigh matters and see them in their true light requires close and attentive study, considerable practice in the interpretation of results, with technical skill. When making experiments it is necessary to know what has been done and how it was done, and for that purpose the ability to read German and French is needed, the bulk of literature being in German.

If in repeating the experiments of another observer the same result is not obtained, it is not necessary to infer that

he is wrong, but rather that some important procedure has been omitted. Peculiarities in the constitution of animals of the same kind may cause different results, as Böhm, at Würzburg, found that aconitia on the frogs there did not kill the motor nerves as Ascharumow stated, but when he was called to Dorpat he found that it did kill the nerves of motion.

Schmiedeberg has discovered that caffein affects the muscles of the rana temporaria, but feebly those of the rana esculenta. One positive fact is worth very many negative ones. In making experiments the operation should be made with the greatest care, time sufficient being taken. One well-directed experiment where all the operative procedures are correct, and the apparatus the best and in perfect order, is worth many slipshod vivisections. The little things are almost of more import than the great ones, as it is only by attentive detail that great ones are carried out. To become a master in the art of vivisection, neatness in operative procedure, care not to injure parts unnecessarily, the most accurate instruments possible at hand, with quietude of mind and temper under the many difficulties that accidentally or unexpectedly arise, are the first essentials.

When a drug is given the local and general action is studied, for to produce a general action the drug must reach the blood and be distributed with it. The poisonous qualities of a drug depend on the amount of it in the circulating fluid. Should the excretion be greater than the ingestion of it in a certain time, then no toxic action will ensue. Should the blood receive it in a greater quantity than is excreted in a given time, then poisoning will result. It is the amount of the drug circulating in the blood in a given time that is the main factor in the production of a therapeutic or a toxic effect. The poison usually reaches the blood either by lymphatic or venous absorption, or by direct introduction into the circulation. Before injecting a substance into a vein, the drug must be dissolved in water. If possible, no alcohol should be used. Acids which coagulate the blood outside

the body should never be injected into a vein. The same applies to any agent acting similarly on the blood. These facts are determined by application of the drug to the blood in a test-tube.

To differentiate, if the nerves are affected directly by the drug, or indirectly by the changes in the blood through the medicines, the experiment of Lewisson should be performed.

It is as follows: A frog is taken, the cerebrum ablated, and glass canulæ are inserted into the bulbus aortæ and vena cava inferior. The aortic canula is attached to a funnel containing three-fourths of one per cent. salt solution. This flows in through the aortic canula and forces the blood out through the canula of the vena cava inferior. If, then, a small quantity of a poison be added to the salt solution, it will soon be seen by the action on the animal if the drug affects the nerves directly.

Animals Used.

In experimentation, the lower animals are chiefly used, such as frogs, rabbits, cats, dogs, pigeons, guinea-pigs, and sometimes sheep, horses, and monkeys. Frogs are readily procurable, cheap, easily managed and disposed of. Their apparatuses are able to survive for some time the destruction of each other, as the heart can be separated from the nervous system without immediate destruction of either, or the lungs may be removed without detriment to the other functions for many hours. Fall frogs are the best for purposes of experimentation. Frogs in the spring and during the period of "heat" soon lose their nerve-irritability, and of course are not desired. It must be remembered that some of our frogs are much larger than those on the Continent. In experiments on the circulation and respiration, rabbits and young cats are quite suitable, as in them the vagus and sympathetic can be easily isolated, as well as the depressors. Albino rabbits whose ears are depilated by chloride of calcium are excellent for the purpose of studying the changes in the

bloodvessels of the ear. In operations of some magnitude, young dogs are best. Dogs are the best for studies of the action of glands, such as the parotid, gastric, and so on. All experiments should be made on a variety of animals before the results can be applied in the study of the functions of man. In observations as to the action of drugs on cerebral functions, man is the best, and the results are the most trustworthy. Some drugs act differently on different species of animals, depending on their constitutional peculiarities.

Animals, Feeding and Preservation.

In blood-pressure experiments the animals should be previously fed on dry fodder. Oats predispose here to coagulation. Rabbits, cats, and dogs should be kept in separate apartments. Frogs are kept by two methods, the wet and the dry. In the wet method you put about fifteen in a flat earthenware pot in a cool place, the water being about half an inch in depth. The pot should be covered with a wire network, which has in its centre a door large enough for the hand to enter. The water must be changed two or three times daily.

In the dry method about a dozen are placed in wet garden-moss contained in a box about a cubic foot in extent. This box must be perforated to allow the water to run through twice or thrice daily to keep the animals clean. The wet method affords better results than the dry as regards mortality. An aquarium, where it can be constructed, is the best.

Fastening of Animals

For dogs, Professor Bowditch, of Harvard Medical School, has invented a simple holder, Fig. 1. It consists of a fork-shaped iron instrument. The points of the fork are united by an iron bar which slips into a hole in one prong of the fork, and is secured at the other end by a catch projecting.

The iron bar is passed behind the canines and bound fast by a strong cord which passes over the jaws. When the iron rod is fastened to the prongs, the handle, B, is inserted into a screw sliding upon an upright rod of a Bernard holder. The holder of Bernard is also a most excellent means to secure dogs of all sizes. Fig. 2 shows it as modified and represented by Cyon. It consists of an iron ring, C, and on its sides are two slits, N N, which have moving in them a semicircular ring, K, with flat sides, the under side being covered with leather, as it fits over the upper jaw of the animal, whilst the under jaw of the animal rests on the

FIG. 2.

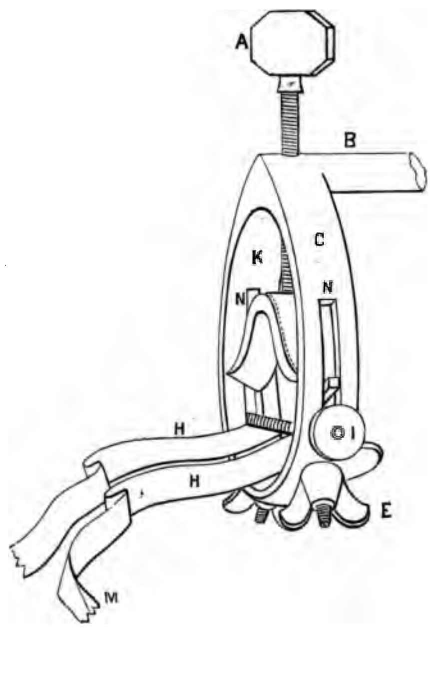
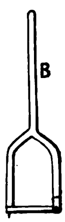


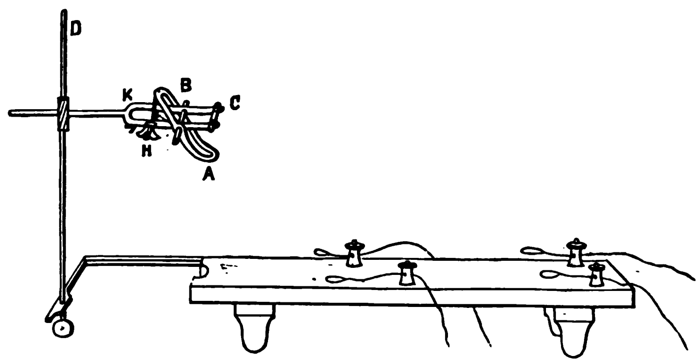
FIG. 1.



lower part of the ring. By means of the screw, A, the snout of the dog can be compressed by the semicircular iron bar, K, according to the size of the dog. In the slits, N,

at their lower part, move two iron plates, H H, fastened by the screws, E. To these iron plates are attached leather straps, M, which pass behind the head and serve to hold the dog from retracting his nose. Cyon has attached a screw-bolt, I, which is passed behind the incisor teeth after the head is fastened. This, like the strap, prevents retraction of the head. The handle, B, is inserted into a nut which moves on a vertical rod. For rabbits there is nothing superior to Czermak's holder, Fig. 3. It consists of a board, in length sixty-one centimetres, width twenty-one centimetres, and

FIG. 3.



height seven and a half centimetres, being mounted on feet. In this board several holes are made along its edge. Into four of these holes are placed little holders, which have cords passing through them, and are fastened to the extremities of the rabbit by a slipknot. The board is covered with a hair mattress. Projecting from the board is a flat iron rod which carries the upright rod, upon which slides a screw arrangement for the reception of an iron contrivance intended to secure the head of the rabbit. It consists of a curved oblong which swings on a movable axis. The part A goes over the nose, grasping it, whilst the rod, B, goes behind the incisors, and the part C beneath the under jaw. By means of the rod, H, and the screw the head is fastened. Then the iron

contrivance is fastened to the forked instrument, K, which is received into the sliding nut on the upright rod.

A larger size is used for small-sized dogs and cats, but frequently cats will be found whose heads are so peculiarly shaped that the iron piece under the jaw presses on the trachea when the instrument is screwed fast to the head, and asphyxiates them. To hold frogs or pigeons a towel wrapped around them generally suffices. For the study of reflex action Professor Bowditch has made a wire support. It consists of copper wire curled on itself like a spring, and the frog has his anterior extremities screwed in between the coils. Frogs can also be fastened to a board by means of five surgical pins, four binding the feet and one the nose. Dr. Tiegel passes a thread through the nose and fastens it, thus avoiding loss of blood.

Physiological Anatomy.

To remove the cerebrum of a frog, take a sharp scissors and cut through the skull on a line with the anterior edge of the membrana tympani, or remove the roof of the skull and divide the cerebrum from the optic lobes.

To divide the medulla oblongata from the spinal cord, wrap the frog's body in a towel, and with the thumb bend the nose down and feel for a slight depression between the occiput and atlas. The incision is to be made on a line with the posterior edge of the membrana tympani. The incision should be made with a sharp-pointed knife, its extent being as small as possible to prevent hæmorrhage. To prepare the gastrocnemius with the nerve attached, called usually the "nerve-muscle preparation," take the frog and open the spinal canal at the medulla, and with a wire thrust destroy the brain and spinal cord, then make an incision through the skin on the back part of the thigh from the knee to the lumbar vertebræ, with the "seeker" (a curve-pointed probe) isolate the nerve from the surrounding tissues down to the knee, divide the spinal column above and below the

exit of the three nerve-trunks forming the sciatic, and with a forceps lift up the bony canal and dissect the nerve out down to the knee; denude the leg of its skin, and cut through the tendo Achillis, isolate the muscle up to its insertion into the femur, cut away the tibia and fibula, and divide the femur at its lower third, which remains attached to the gastrocnemius. The sciatic attached to the gastrocnemius must not be injured. To lay bare the vagus, a glass tube is pushed down the œsophagus of the frog, so as to stretch the tissues and bring the parts into view. The sternum is divided, and the posterior horn of the hyoid bone is sought for. From here runs the petro-hyoid muscles, and their lower edge is the point to find the vagus. Over these muscles run the hypoglossal and glosso-pharyngeal nerves, which are divided. The laryngeal nerve is also found, and is divided. It must not be mistaken for the vagus. In the rabbit, to find the vagus, the skin at the upper end of the trachea is taken up between the fingers and denuded by means of a scissors; the fascia divided, and the sterno-cleido-mastoid drawn aside; when the carotid artery is brought into view with its three nerves, vagus, sympathetic, and depressor. In dogs the vagus and sympathetic are firmly united; the depressor in the rabbit springs by one branch from the vagus, and by another from the superior laryngeal. To find the superior laryngeal, incise from the trachea towards the angle of the jaw, then pull aside from the trachea the muscles, and seek the thyro hyoid membrane, where the tortuous trunk of the nerve will be found to give off some branches. To find the splanchnics, the suprarenal capsules are sought; the left splanchnic is just above the left suprarenal capsule on the front of the aorta, and the right somewhat farther away from the aorta, over the vena cava. For reference in dissection, Cyon's* atlas is the best guide, as it contains numerous plates of physiological anatomy.

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* Atlas zur Methodik der Physiologisch. Experimente und Vivisection. Von E. Cyon, Giessen, 1876.

ANÆSTHESIA.

To abolish consciousness, chloroform, ether, chloral, and morphia are used. Laudanum or morphia by the vein acts admirably with dogs and cats, but is uncertain with rabbits. Chloral acts well with rabbits, narcotizing them. When this is given, heat will not excite reflex action, but touch will. Chloral reduces the respiration and cardiac movements by an action on the centres of respiration and the heart itself, also diminishing the arterial tension. Morphia increases the irritability of the centres and ends of the vagi, of the motor and sensory nerves, and then reduces it. Reflex excitability is also increased and then diminished by it. Chloral is excellent for frogs, as opium or morphia tetanizes them. Chloroform is also very useful. It excites and then depresses the functions of the nervous system, especially the nerve-centres. Cyon states that it excites greatly the vagi by a direct action on them, and not by irritation of the sensory nerves, thus reflexly calling out increased inhibitory action of the ganglia of the vagi. To administer chloroform to frogs, cats, mice, pigeons, and guinea-pigs, it is convenient to put them under a glass jar, and then to introduce a sponge wet with a few drops of chloroform. Care must be taken to allow some air to enter. Bernard has constructed for dogs an inhaler which consists of a tin cylinder covered with leather, which passes over the nose and is retained by strips of extensible material which is fastened behind the head. This cylinder is closed at the other end by a sieve-like arrangement of thin wire. On the first tin cylinder fits another tin cylinder containing a sponge which receives the chloroform. This cylinder is also closed by a wire network which admits the air. The most internal wire network prevents the sponge from blocking up the nasal passages. Great care must be taken or death will result either by arrest of the respiratory centres or the heart itself. Woorari is another agent which is able to render

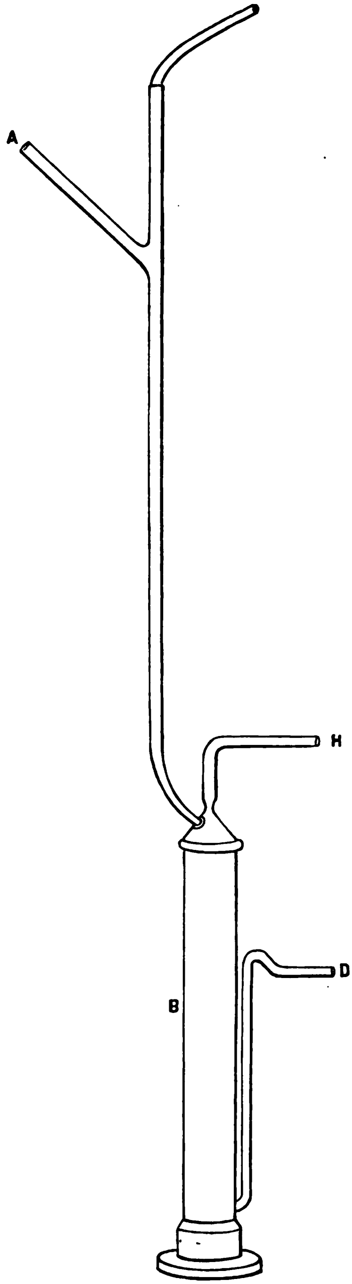
animals immovable. This is accomplished, as Dr. S. W. Mitchell has proven, by a paralysis of the motor nerves, leaving the sensory nerves and sensory ganglia intact. For dogs the dose of chloral is five grammes by the vein, divided into three doses; of morphia by vein, .05 gramme; of laudanum by the vein, forty minims. For rabbits the dose of chloral subcutaneously is one gramme; of morphia by the vein, .008 to .015 gramme. For frogs the dose of chloral is .025–.05 gramme, subcutaneously. The dose of woorari must be determined for each specimen, care being taken to use only small doses, as large doses paralyze the vagi. When to use and not to use anæsthetics is an important question, which must be decided by the action to be studied.

Artificial Respiration.

For this purpose I used a column of water in the Physiological Laboratory of the University of Pennsylvania. The water rushed from the usual water-pipe of the city past the open tube, A, Fig. 4, to the receiver, B, about twenty-five feet below. This receiver has an exit-tube, D, for the water to flow out, and near its top another tube, H, which conveys the air caught by the fall of water back to the laboratory. The water passing by the open tube, A, sucks in air, which passes down with the water into the receiver, where, being unable to escape, it flies up the tube, H, in a constant stream. By means of rubber tubing the air was carried to the operating-table from the tube, H. A weight weighing about a pound was allowed to fall on the rubber tubing, and to be lifted from it at regular intervals by means of a magnet, through which an electric current passed at intervals, by means of a metronome carrying a pen, which dipped in and out of a cup of mercury. Four large carbon-zinc cells generated the electric current to raise the pound weight. By regulating the rapidity of the metronome the current of air passing into the chest of the animal can be broken as often as is desired, the breaks being according to the normal res-

pirations of the animal operated on. This apparatus worked exceedingly rhythmically, and run for about two hours. Air is driven in Ludwig's laboratory with great regularity by a gas motor. If no other apparatus is at hand, a bellows may be used, its movements being made regular by listening to the beat of a metronome. The extent of its movement must be regulated by a graduated check. The bellows may be run by a water motor or by a crank and eccentric attachment.

FIG. 4.



MEASUREMENT OF TEMPERATURE.

To measure temperature, Fahrenheit's instrument is employed, although the Centigrade would be much better for immediate comparison with the measurements abroad. No instrument should be relied on for correctness unless tested by a normal thermometer. Walferdin has invented a thermometer called metastatic. It is filled with quicksilver, and can be used to estimate all kinds of temperatures, but must be compared with a normal thermometer. It is capable of giving the

$\frac{1}{100}$° C. To measure the temperature of deepseated tissues, as the interior of the heart and large veins, the instrument of Heidenhain is employed. It consists of a short thick part and a long thick-walled capillary tube, which is graduated to $\frac{1}{10}$° C., and is so made that by practice $\frac{1}{100}$° C. can be read. It might be expected that this tube would cause coagulation or considerably interrupt the blood-current, but in practice these things did not take place. When it is used woorari must be given, as the instrument is easily broken.

To take the rectal temperature Heidenhain has constructed a thermometer with the capillary tube bent at right angles. In the estimation of rectal temperature, Kussmaul and Tenner have shown that the animal must not be bound down, as the temperature falls. The animal can be wrapped up in a piece of cloth so as to render the extremities immovable, or put into a box which is partially covered. To estimate the temperature of the different parts of the body, a thermopile may be used; it consists of elements of bismuth and antimony, and is connected with a galvanometer whose needle-deviation shows which part is the warmer. To estimate the amount of heat developed by a muscle, Heidenhain has constructed a lever arrangement by which the muscle during its contraction is kept constantly against the thermopile.

Time-measuring Apparatus.

To measure time a metronome is very useful. Its shape is like that of a pyramid, and when its front cover is removed a pendulum carrying a weight swings to and fro, its rapidity being sixty per minute when the weight is pushed up to the number sixty on the scale behind the pendulum. By elevating or lowering the weight the pendulum beats faster or slower, the number of beats being closely estimated either by the scale or by the watch. To keep the pendulum in vibration there is a stiff spring near the base of the apparatus which is wound up by a key like a clock. By means of a cog arrangement the pendulum moves a clapper

which strikes a bell every few seconds, making the time audible at a distance. The numbers on the lever, at the side which pushes in and out, show how often the bell strikes; two, denoting two pendulum vibrations; six, six pendulum swings. By attaching to the pendulum a wire which has two prongs like a fork, and each prong dipping into a separate cup of mercury, an electric current can be opened and closed, the current on closing passing from one cup to the other through the wire prongs, when it dips into the mercury; the current is broken when they leave the cups. Professor Bowditch took off the bell and attached a watch-spring to the clapper. The spring passes out of the box through a hole, and is bent at right angles to itself. Its point then dips in and out of a cup of mercury, the current passing through a wire attached to the lever on the side containing the numbers, and through the watchspring into the mercury, closing the current. This instrument is used to regulate the rhythm of a bellows in artificial respiration, to break and open electric currents so as to have the muscle irritated so many times a minute, or to run an electro-magnet marking seconds by a lever on a smoked surface, and to count the time for reflex action. To measure time there is usually employed a drum called Young's cylinder. This cylinder is composed of metal, and is covered with a glazed paper which is smoked over a coal-oil lamp. To run the cylinder, that is, to make it revolve, there is employed either a strong spring or weights. Fig. 14 represents such an arrangement, called Ludwig's registering apparatus. Dr. Locke, of Cincinnati, was the first to make use of electric chronographs. The electro-magnet is made of a U-shaped piece of iron covered with coarse wire. Now when a current is passed through this wire, the iron becomes magnetized and draws the vibrator bearing the armature towards it. A pen attached to the armature rests against a smoked drum, and when the armature moves the pen registers this movement. If the pen is parallel to the drum the closing of the current will draw up the iron armature, the pen pro-

ducing a vertical line. When the current is broken a wire spring pulls down the armature to its original position, the pen making another vertical line in its descent. If the current is broken every second, the distance between the vertical lines will represent the rate of movement of the drum during that time. To close and open the electric current a metronome or pendulum is very useful. Ludwig has invented a very excellent instrument to close and open currents, called Unterbrechungsuhr. It consists of a pendulum swinging back and forth, rotating a disk covered with projecting points. The entering current passes through these points, which sweep past a curved rod, and through this to the magnet. By an ingenious mechanical contrivance the curved rod can be slid along on an axis, the points on the disk being so arranged that the current can be broken every one, two, or four seconds, and so on, by simply sliding the curved rod on its axis. A chain and weight, as in clocks, keeps the pendulum moving. Another means to measure time is the tuning-fork. Those which register $\frac{1}{60}$th and $\frac{1}{240}$th of a second are the most suitable for physiological purposes. They have a very light flexible pen attached to one of the prongs. The handle of the tuning-fork being firmly fixed, a horsehair bow is swept over the fork and sets it in vibration. If now the pen rests against a smoked revolving surface, a line formed of many zigzags will be seen. Each zigzag, Fig. 8, H, represents the fraction of a second, and by simply counting them the rate of movement of the drum is determined.

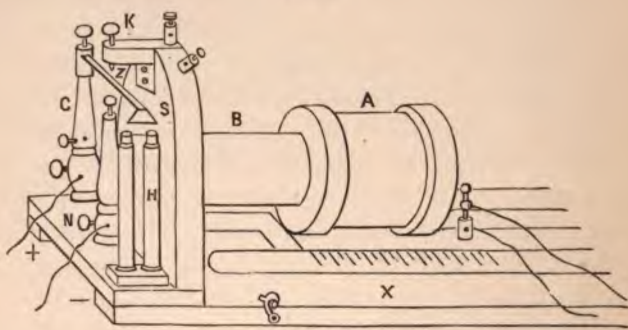
To determine if the forks register correctly, the registrations may be made below each other, and if the curve of the fork recording $\frac{1}{60}$th of a second is equal in length to four of the curves of a fork recording $\frac{1}{240}$th of a second, then it may be inferred that the forks record accurately. An electro-magnet is a much better instrument to run the tuning-forks than a horsehair bow. Marey's electro-chronograph, registering $\frac{1}{100}$th of a second, is excellent.

Electrical Apparatus.

To generate electricity several varieties of galvanic elements are employed. The one most frequently used is the Grove cell. It consists of a porous cup filled with concentrated nitric acid. This cup is inclosed by a zinc cell resting in a solution of sulphuric acid of the strength of one part acid to five parts water. In the nitric acid a piece of platinum rests. This cell is very constant in its action. Another galvanic cell, which contains no acid, and consequently causes no destruction by its presence, is the Leclanché. It consists of a porous jar filled with peroxide of manganese inclosing a carbon cylinder. The porous jar is surrounded by a glass receptacle filled with a saturated solution of muriate of ammonia. Into this solution dips a zinc rod. For the proper care of the Grove cells, the porous cups after use should be allowed to soak in a trough of water. The zinc must be kept well amalgamated by the following solution: one thousand parts of a mixture composed of one part nitric acid to three parts hydrochloric acid, in which two hundred parts of mercury are dissolved by heat; add to one thousand parts of hydrochloric acid. When the Grove cell is in use it should be placed outside the window, in a covered wooden box, perforated for the escape of the fumes. This is done to prevent the acid acting on the fine instruments in the laboratory. The wires running from the cell through the window should be insulated. The induction apparatus employed in all physiological laboratories is that of Dubois-Reymond. It is composed of two spirals, the first being filled with thin iron wires, each one being isolated by shellac varnish. The strength of the induced current is graduated by sliding the secondary spiral, A, to or from the primary spiral, B. The distance between the spirals is divided into millimetres, and when it is said the nerve is irritable, at say fifty millimetres, it means that when the secondary spiral is standing at fifty millimetres on the scale, X, along the grooved track, the induced current of the secondary

spiral is just sufficient to make the muscle contract upon the irritation of its nerve. Prof. Adolph Fick, of Würzburg, has graduated this instrument by means of a galvanometer in what he terms electrical units. This graduation is used when it is necessary to study the relation between the intensity of the current and the height of muscular contraction. When the secondary coil is placed at ten on the galvanometer scale, it is expressed by ten units, and when the spiral is pushed to twenty units, the strength of the electrical current is doubled. Professor Bowditch has done away with the sliding of the secondary spiral, by causing it to rotate on its own axis at an angle to the primary spinal. The rhythmical opening of the current from the battery through the primary spiral is accomplished by the automatic electro-magnetic hammer. The current leaves the battery and enters by the brass support, C, Fig. 5, carrying the vibrator, having an ar-

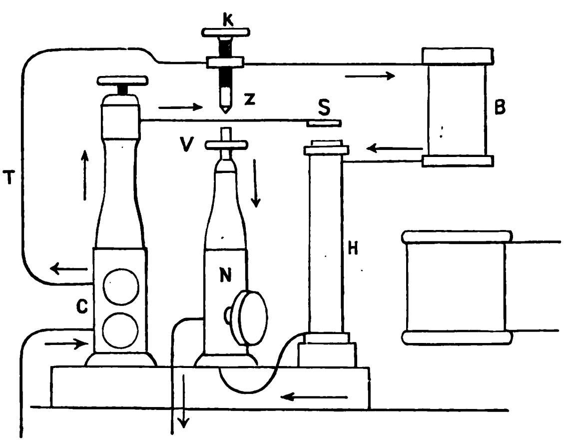
FIG. 5.



mature at S, through the vibrator till it meets a small platinum plate, against which presses the platinum point, Z, of the screw, K, by the elevation or depression of which the play of the spring may be retarded or accelerated. From the platinum point, Z, the current enters the primary spiral, B, and then into the electro-magnet, H, back to the battery by the pole, N. The moment that the current enters the electro-

magnet, it magnetizes the soft core of the latter, which draws down the armature, S, interrupts the contact between the vibrator and the platinum point, Z, and thus breaks the current. The moment the current is broken the spring flies back, the current is again closed, and so the vibrator is kept in constant motion. By this arrangement the physiological strength of the opening shock is greater than that of the closing. To equalize them and to prevent unipolar action, Helmholtz has arranged matters as in Fig. 6. The armature,

FIG. 6.



when it is attracted by the electro-magnet, does not as in the previous figure open the current, but closes an accessory circuit, which diminishes the strength of the battery current in the coils of the electro-magnet. The accessory current is closed when the platinum plate on the vibrator touches the platinum point, V. The vibrator in this arrangement moves more slowly. The current in Helmholtz's arrangement enters the brass support, C, and the whole of the current at first enters the wire, T, Fig. 6, the primary coil, B, and the electro-magnet, II, whose soft iron becoming magnetic draws down the armature, S, the vibrator thus being brought into contact with the screw, V. This creates a

circuit much shorter than that through the primary coil, B, so that a large quantity of electricity goes up the brass support, C, and through the vibrator and screw, V, down the pillar, N, to the battery. The screw, K Z, is elevated in this arrangement so that it does not, as in Fig 5, touch the platinum plate on the vibrator when it moves. Here the vibrator only strikes the platinum point on the screw, V. By the closing of this shorter circuit, the electro-magnetic current is weakened, the soft iron is mostly demagnetized, and the armature flies up with the vibrator. For the application of the induced current to tissues, electrodes are used, those of Ludwig being the best. They consist of two copper wires inclosed in an ivory handle with flexible wires uniting them to the secondary spiral, A, Fig. 5. Electrodes set in gutta-percha, with a slide of the same material covering them, and the nerve lying on them, have been made. They are excellent to prevent desiccation of the nerve. All these electrodes are polarizable.

It happens that the constant current is also used to excite nerves. To prevent polarization Dubois-Reymond has invented non-polarizable electrodes, which are formed of flat glass tubes, whose lower end is plugged up with common salt clay, which is moulded into a sort of curved point to hold the nerve lying on them. These glass tubes are each connected by a bent arm, with a piece of brass ending in a ball-and-socket joint of a support. From this brass piece projects a horizontal piece of brass upon which is fastened a slip of amalgamated zinc, immersed in a concentrated solution of the sulphate of zinc, which is contained in the glass tubes.

To open and close the galvanic current the key of Dubois-Reymond is employed. It consists of a rubber plate, which by means of a screw arrangement can be screwed to any table. On the hard rubber plate are two brass bars perforated with holes, and containing screws which fasten the wires. When the key is down the brass bars are connected by their brass point, and the current is closed. When the key is up the current is broken.

MEASUREMENTS.

In the measurements employed in the laboratory those of the French are generally used.

The weight of a cubic centimetre of water at 4° C., equal to 16.9 minims Imperial measure, is called a gramme, which is divided as follows:

		Troy grains.
10 milligrammes form 1 centigramme, . .	=	.15434
10 centigrammes form 1 decigramme, . .	=	1.5434
10 decigrammes form 1 gramme, . . .	=	15.434
A kilogramme, ...	=	15434.0234

The metre is divided as follows:

		English inches.
10 millimetres, ... form	=	.039371
1 centimetre, ...	=	.39371
10 centimetres form 1 decimetre, ...	=	3.93710
10 decimetres form 1 metre, ...	=	39.37100

The litre is divided as follows:

		Apothecaries' measure.
10 millilitres, ... form	=	16.2318 minims,
1 centilitre, ... 10 centilitres form	=	.27053 fluid drachms.
1 decilitre, ... 10 decilitres form	=	3.3816 fluid ounces.
1 litre	=	2.1135 pints.

The balances needed in a laboratory are usually two ; one to weigh at least from a milligramme up to a hundred grammes, and another to weigh from a gramme up to the weight of a man.

CANULÆ.

Canulæ are usually made either out of glass or metal. The glass canulæ are made by drawing glass tubing to a point in the flame of a blowpipe, a slight bulge being made near the point for the ligature to catch. To insert either a

metal or glass canula into the carotid the following procedure is necessary: The animal is bound down, the hair clipped off, the skin pinched up and divided by a sharp scissors. Then with a blunt forceps take up the fascia and divide it with the scissors. After this take a blunt instrument, slightly curved at the point, called a "seeker," and gently tease away the connective tissue from the artery, the muscles being previously held aside by hooks, loaded with weights, by means of a cord. The artery being bared, a clip is placed on it and a ligature thrown around the artery by a curved ligature-holder, on the distal side of the clip. Between the ligature and the clip a second ligature is passed, and a V-shaped snip is made by a finely pointed scissors into the artery. Then the canula is pushed in towards the heart and bound there by the ligature. When the clip is removed the blood will be propelled through the canula, which may be (after being filled with soda solution) put in communication with a mercurial manometer. When a canula is inserted into a vein, it must be filled with the fluid to be injected before the clip is removed. The external jugular vein is usually preferred for injection-purposes. The metal canula, Fig. 14, I, has a little ring attached, through which the ends of the ligature pass so as to hold it in place.

To convey air into the chest after poisoning, canulæ are inserted into the trachea. For the rabbit Ludwig has invented a very ingenious one, Fig. 14, Y. It is a hollow vertical tube having at right angles two other tubes, the one, A, being inserted into the trachea, the other, B, being joined to the tube of the respiration-apparatus by means of rubber tubing. The end in the trachea has a small line of depression to allow the ligature to press in and thus retain the instrument. At O is a hole to allow the expired air to pass out. The tracheal end of the tube can be rotated on the vertical tube.

In glass tracheal canulæ, a hole is made in the side of the canula for the escape of expired air.

ADMINISTRATION OF MEDICINES.

The animal should be first weighed, then fastened. To introduce medicines by the stomach, a gum catheter is very convenient. In the case of dogs a block of wood may be inserted into the mouth, and through the hollow centre the catheter introduced into the stomach. When a medicine is introduced subcutaneously, the hypodermic syringe will suffice, the substance being introduced in the flanks of the animal. As absorption is slow either subcutaneously or by the mouth, the drug is frequently injected directly into the circulation through a vein. The drug may also be changed by the liquids of the stomach or connective tissue. Before any drug is injected into the blood, it should be known that it does not coagulate the blood, precipitate its elements, or in any way interfere with its circulation.

To inject a medicine, it is dissolved in water, and the solution tested to see if it is neutral. Alcohol must be avoided as a solvent, for it would confuse the effects due to the action of the drug. The solution being prepared, the canula inserted into the vein and filled with the solution to be injected, the nozzle of the syringe containing the solution accurately fitted into the canula and the clip removed, the substance should be slowly injected. No air should be allowed to enter. Some birds, like pigeons, have an immunity to atropia, as has been shown by Prof. H. C. Wood. Gases can be administered, if dissolved in water, by injection, but inhalation by the lungs is the best method. A rubber balloon containing the gas may be fitted over the nose of the animal, or a wide-mouthed bottle containing mercury, into which a glass tube dips, and having an exit-tube in the stopper, may be used. Here the balloon containing the gas is attached to the tube dipping into the mercury, and from there passes through the exit-tube into the tracheal canula, which may be made of glass and bifurcate, one branch connected with the gas and bottle arrangement, the other branch with the respiration appa-

ratus. The respiratory branch must be fitted with a hole for the exit of air expired. If a vaporous fluid is used, it may be placed in the bottle over the mercury, and the air for respiratory purposes driven through it.

The mercurial bottle prevents air from returning, and is known as Müller's valve.

Another means, which is very useful, is to have a bottle with metal top containing a metal stopper. The metal top is perforated at opposite sides by two holes; the metal stopper is perforated by two tubes in its base and two tubes through its side; the two tubes through the base of the stopper communicate with one of the tubes through the side at right angles. The side tubes of the stopper, by its rotation, can be placed in connection with the two tubes entering the metal neck. By one method the air is driven directly through the stoppers, but by revolving the stopper the air is driven into the bottle and then out of it If, now, a vaporous liquid is placed in the bottle, it can be driven by the air into the lungs, or be excluded at pleasure by revolving the metal stopper. Having administered the medicine in a large dose, note whether it convulses or paralyzes; whether the respiratory or cardiac apparatus stops first; if there is emesis or catharsis; upon what system the drug acts most decidedly, the nervous, cardiac, or respiratory; if the mode of administration by the stomach or subcutaneously produce any difference in its action; the smallest dose that will kill if the drug is toxic; the relation of the lethal dose to the weight of the animal; if the drug is excreted by the kidneys, and so on. All the symptoms should be noted on paper at the time they happen. The general action of the drug having been determined, the changes in the nervous system, circulatory apparatus, and so forth, are to be studied.

Antagonism of Drugs.

In studying the antagonism, the following points should be aimed at: First, the dose of each drug that will be just

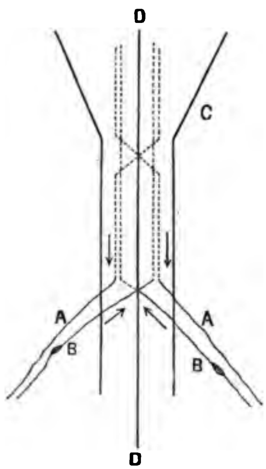
sufficient to kill, and the relation of it to the weight of the animal. Secondly, the action of the antagonizing drug on the poisoned animal. Thirdly, the action when both are simultaneously administered. Fourthly, the action of the poison when the antidote has been previously given and absorbed.

CHAPTER II.

ACTION ON NERVOUS SYSTEM.

THE spinal cord consists of white and gray matter, the latter being the seat of reflex action. The motor fibres run up the cord on the side that they enter, and cross to the other side in the medulla oblongata. The sensory fibres nearly all cross over from the point of exit to the opposite side of the cord, and thus traverse the cord. Brown-Séquard gives the following diagram of their course, Fig. 7: A A are motor nerves which pass up the cord and decussate in the medulla. B B represent the sensory nerves, which decussate in the spinal cord and not in the medulla. D D is a median line, dividing the cord into two halves. When the sensory nerve-endings in the skin are pinched, the impression is conveyed to the spinal sensory ganglia, from them by commissural fibres to the spinal motor ganglia, and thence down the motor nerve, which causes the muscle to contract. Such a movement is called a reflex action, and all such movements are involuntary. Certain poisons, like strychnia, thebain, gelseminic acid, increase this reflex activity, causing tetanus, whilst others, like chloroform, diminish it. In the corpora quadrigemina and thalami optici are seated ganglia which inhibit spinal reflex activity, as when an animal is decapitated, reflex activity in the spinal

FIG. 7.



cord rises. These ganglia are called Setschenow's.* The cerebellum is thought to be the co-ordinating centre of voluntary movement, and, according to Ferrier, the centre for the co-ordination of the movements of the eyeball. Alcohol, according to Flourens, produces want of co-ordination by affecting the cerebellum. The cerebrum contains ganglia which are the seat of the will, thought, and consciousness, and by the latest researches it also contains ganglia which control the various movements of the body. The pupil is under the control of two nerves, the oculo-motor, which supplies nerves to the circular fibres of the iris, the sphincter pupillæ; the sympathetic, which carries nerves to the radiating fibres, the dilator pupillæ. When the ends of the oculo-motor in the circular fibres are paralyzed, as by atropia, the pupil dilates, and when they are irritated by Calabar bean they contract. When the sympathetic is irritated, the pupil dilates. The fibres in the cervical sympathetic, which go to the pupil, arise in the medulla spinalis, the "inferior ciliospinal centre of Budge." The submaxillary gland has its secretion increased by irritation of the chorda tympani, and decreased by the excitation of the cervical sympathetic. The blood in the arteries of the gland runs more rapidly, and the veins pulsate when the chorda tympani is irritated, because it contains vaso-dilator nerve-fibres, which allow the bloodvessels to dilate. When the vaso-constrictor fibres in the sympathetic are irritated, the current of blood in the gland is slowed, and the blood from the veins is dark. This increase and decrease of secretion is produced by a direct action of the nerves on the gland. Atropia paralyzes the secretory fibres, but not the vaso-motor in the chorda tympani. The paralysis of the secretory fibres is the reason that the throat is dry in using atropia. This atropia paralysis can be removed by Calabar bean, which causes, in addition,

* I have lately made experiments which make it probable that there are ganglia in the spinal cord inhibiting reflex action, and spinal vaso-motor centres. Setschenow has held that there are spinal centres inhibiting reflex action.

increased secretion, by irritating the endings of the chorda tympani in the brain. Nicotin and digitalin act like physostigma, but in large doses nicotin paralyzes the chorda tympani. Jaborandi increases the salivary secretion by peripheral irritation of the chorda tympani. Respiration is carried on by the want of oxygen in the blood, which irritates the respiratory centres; these send their motor impulses through the phrenic and other spinal-motor nerves, and set the respiratory muscular apparatus into action. The pneumogastric endings in the lungs, and the sensory nerves in the skin, are the main conveyors of impressions to the respiratory centres. Hering and Breuer have shown that the pneumogastric conveys impressions which call out both inspiration and expiration. Impressions carried by the superior laryngeal throw the diaphragm into relaxation. Both these nerves carry the impressions towards the brain, that is, they call out reflex acts. Certain drugs, like lobelina, accelerate the respiratory movements by irritating the peripheral end of the pneumogastrics. Many poisons, like gelsemina, kill by paralyzing the respiratory centres themselves. Other poisons, like woorari, kill by paralyzing the motor nerves concerned in movements of respiration.

Intestinal Movements.

When the splanchnics in the abdominal cavity are exposed and irritation applied to them, the intestinal movements are arrested by an inhibitory action.

Temperature.

The origin of the heat of the body is thought to be in molecular changes of the tissues. Professor H. C. Wood, Jr., believes that in the pons varolii or higher there is a nervous centre which inhibits the production of heat. The vasomotor nervous system plays quite a part in the regulation of temperature.

Renal Excretion.

Ludwig has proven that an elevated blood-pressure is an

important factor in the secretion of urine. Increased arterial tension causes an increase of the renal secretion. Cold applied to the skin, and the ingestion of liquids, is believed to excite the kidneys to increased action by elevating the arterial tension. Digitalis is thought to act as a diuretic by increasing the blood-pressure.

Action on Motor Nerves.

To study the action of a drug on the nervous system, the effect on the motor nerves is very frequently first observed. As atropia has been very extensively experimented with, I will take for illustrations experiments from the authors, Botkin, von Bezold, Fraser, and Keuchel, who have studied the action of this medicine. I believe that if the student will repeat these experiments he will soon be prepared to engage in original investigations of this nature.

Experiment 1.

Two frogs, as nearly alike as possible in size and species, are selected and fastened. Then the sciatic nerve of each is severed high up, and placed on two pairs of electrodes connected with the secondary spiral of Dubois's induction-apparatus. Only one of the frogs is poisoned; then at intervals of five minutes the irritability of the nerves is tested. In this experiment no injury must be done to the iliac arteries carrying the blood to the ends of the motor nerves.

Time.	A. Normal.	B. Poisoned.
3.45 P.M., . . .	32	40
3.50 P.M., . . .	31.8	34.8—.01 gr. of atropia sulph. subcutaneously injected.
4.00 P.M., . . .	44	30
4.03 P.M., . . .	43.7	29.8
4.05 P.M., . . .	43.9	29.7
4.10 P.M., . . .	44.2	31
4.15 P.M., . . .	43	30.5
4.35 P.M., . . .		30
4.47 P.M., . . .	39.2	30
5.02 P.M., . . .	39.5	28

As is seen by an examination of Experiment 1, and the numbers in the colums A and B, the poisoned sciatic is constantly being reduced in irritability. Now, this reduction of irritability may have its seat in a lessened irritability of the muscle. To decide, the next experiment is performed.

Experiment 2.

A frog received 0.2 gramme of atropia subcutaneously. Within five minutes there was no reflex action by irritation of cutaneous nerves. An hour afterward the irritability of the sciatic, with the gastrocnemius attached, was compared with a normal one.

	A. Poisoned.	B. Normal.
Irritation of the sciatic, farthest point from the muscle, ...	29	44
Irritation of sciatic, near the muscle, ...	22	34
Direct irritation of muscle, ...	21	23

To prevent desiccation of nerves and muscles in this experiment, they are wet with a one-half per cent. salt solution. As the experiment shows, the irritability of the muscle is not attacked by the doses of atropia used, so that the conclusion follows that the irritability of the motor nerves is diminished.

Larger doses of atropia kill the motor nerves, as is seen in the following experiment:

Experiment 3.

A frog received 0.3 gramme of atropia subcutaneously. An hour afterward the sciatic was tested with strong induction-shocks, and it was completely unirritable. The muscle possessed its normal irritability.

If a drug produce muscular twitchings, you amputate the leg, and if they persist, they are peripheral in origin, and due either to irritation of motor nerve ends or the muscular

tissue itself. You can also inject into the artery of an extremity the drug, and then test the irritability of the nerve, and also observe if convulsions or twitchings occur. Kühne has given an ingenious method to decide if a drug acts on the muscle or the end of the motor nerve. In the neighborhood of the tendinous ends of the sartorius of a frog, the parts are free from nerves, the nerve being in the middle of the muscle. Now, by testing with a Dubois-apparatus, the irritability decreases from the centre of the muscle towards the periphery, because the nerve is more easily excited than the muscle, the former being more irritable. If, now, a sartorius muscle is removed from the poisoned frog, and the irritability of the middle of the muscle does not exceed or is less than that of the ends of the muscle, the inference is that the drug acts on the ends of the motor nerve.

Action on the Muscle.

Here you take a frog, remove the cerebrum, and dissect out the gastrocnemii, and place one in a 1 per cent. salt solution, and the other in the solution containing the poison. At intervals their irritability is tested by electrodes separated as widely as possible.

Experiment 4.

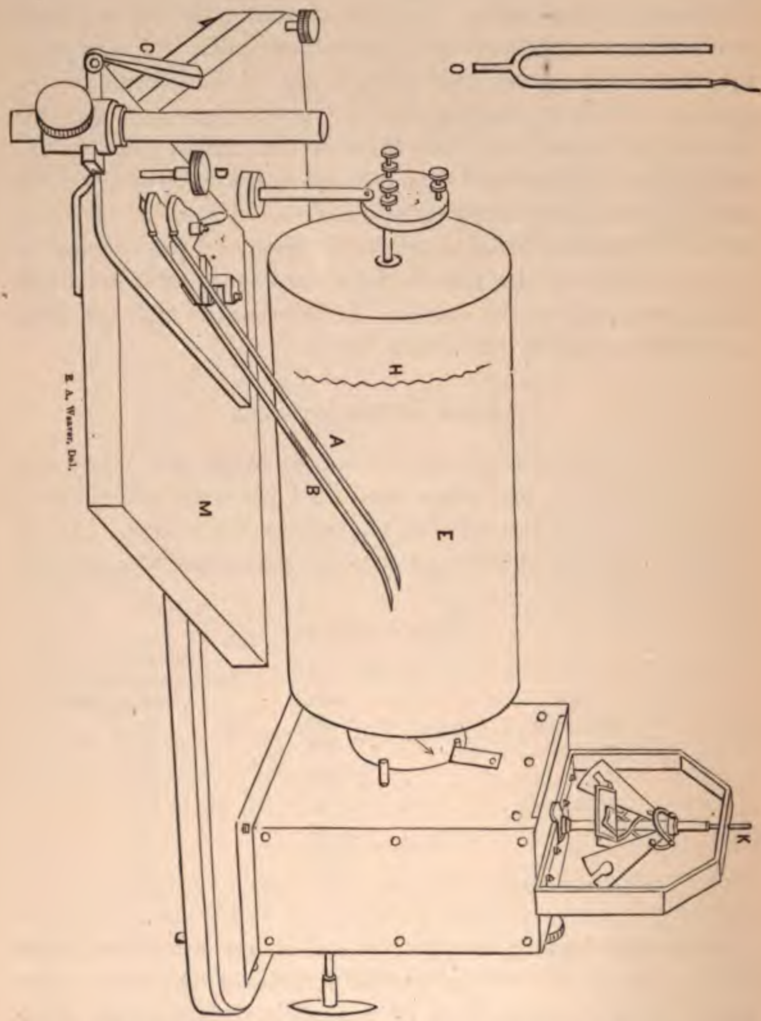
Time.	Normal.	Poisoned by Sanguinarinæ sulph.,* 1 c.c. = .025 gramme.
10.45 A.M., ...	27	27
10.47 A.M., ...	27	23
10.50 A.M., ...	27	21
10.55 A.M., ...	27	12
10.57 A.M., ...	27	9
11.00 A.M., ...	27	3
11.10 A.M., ...	27	0

As is seen locally, sanguinarina destroys muscular irritability. To study the height and form of the curve produced by the contraction of a muscle, instruments called

* Dr. R. M. Smith, Sanguinarina, A. M. Med. Jour., October, 1876.

myographs are employed. Fig. 8 represents the comparative myograph of Marey. It consists of two levers, to each

FIG. 8.



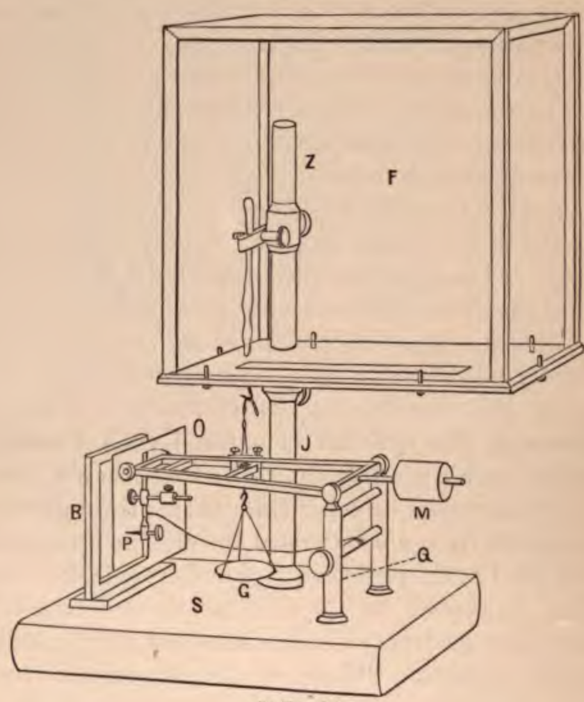
of which the tendo Achillis of a frog is attached. At one end the levers carry aluminum pens, A, B; at the other end

springs are attached, which being in contact with the eccentrics are so adjusted as to cause the muscles to overcome greater or less resistance during contraction. At C is a lever to elevate the levers from inscribing on the smoked cylinder. At D there is a screw, which regulates the pressure of the pens on the drum. E is a cylinder which carries the smoked paper to receive the tracings. This drum is kept in revolution by means of a strong clockwork, and its motion is made rhythmical by a regulator. This instrument, called Marey-Foucault's regulator, has three axes on which the drum may be revolved with different rapidities. H is the curve of the tuning-fork, O, which registers the rapidity of the movement of the drum, or the length of time it takes a muscle to contract. The regulator can be used either in horizontal or vertical position. When a very great rapidity in revolution is needed, a glass disk is fixed on the axle, K, which bears the regulator. This disk is necessary in measuring the rapidity of the transmission of nerve-force. When using the myograph, the cylinder is covered with glazed paper and smoked by a coal-oil lamp. The frog has his brain and spinal cord destroyed by means of a thrust through the cerebro-spinal axis, from a wire passed through an opening of the vertebral canal at the posterior edge of the medulla oblongata. A ligature is applied to the iliac artery and vein, and the tendons of the gastrocnemii are attached to the levers by means of little hooks, sliding on the levers, and thread or fine wire. Then the frog is poisoned, and the curves of the muscles are taken. The levers being directly superimposed, give the curves side by side, so that any variation in the muscle-curve by a poison may be discovered. To irritate the muscle, the poles are carried usually to the sciatic nerves or the muscles themselves, by means of electrodes supported by lead wire, which allows them to be moved in any direction. The frog is fastened to the cork table, M, by means of strong pins.* After the muscles have registered

* The Villarceau regulator is better than the Foucault, giving a more uniform motion.

their contraction, the smoked paper is dipped into an alcoholic solution of rosin, which fixes the tracing. Fig. 9 represents the myograph of Pflüger. It has a mahogany base,

Fig. 9.



from which rise two brass columns, A, between which plays the marking lever, P, which has fastened to it by means of a hook, the tendon of the gastrocnemius of a frog. The other end of the muscle is secured by a clamp sliding on the brass rod, Z, and upon which the moist chamber, F, can also slide. To weight the muscle, the scale-pan, G, is fastened to the lever attached to the muscle. The pan is counterpoised by the weight, M. A blackened piece of plate glass, O, moves in the frame, B. When the muscle contracts it

moves the style, P, which registers the height of the contraction on the sooted surface of the glass, O. Then when another contraction is to be registered, the glass is pushed laterally a few millimetres. This instrument is also made with two levers registering side by side, and when the form of the curve is to be studied, a revolving drum receives the marking instead of the glass plate. These double levers permit the gastrocnemii to be fastened and acted upon by a poison, as was the case with the comparative myograph of Marey. The moist chamber, F, is kept so by a little sponge in it saturated with solution of chloride of sodium. It has an opening in it through which the muscle is attached to the lever work. It will be noted whether rigor mortis appears, and when, how long it remains, the reaction of the muscle, its color, and so on. Should the muscle show a prolongation of contraction as in the following figure, Fig. 10,

FIG. 10.



Action of Papaverin on striated muscle.

study the time of contraction after direct irritation or indirect irritation, the effect of different strengths of electric irritation on the muscle curve by ascending and descending induction currents, the effect of repeated successive induction shocks either through the nerve or muscle on the prolongation of the muscle-curve; also the effect of irritating the muscle or nerve at various intervals of time, on the length of the prolongation, the laws of electrotonus of the nerve-muscle preparation, the effect of an opening and closing ascending or descending constant current on the time of contraction, using here Dubois's rheocord and his non-polarizable electrodes, and the amount of negative variation as shown by the galvanometer. To seek out the seat of this prolongation, irritate

the nerve successively at different points as well as the muscle, and observe the amount of prolongation. Or poison the frog with woorari, irritate the muscle directly, and observe the amount of prolongation. The woorari kills the intramuscular nerve endings. To study the amount of heat evolved by the veratrinized muscle during contraction, employ Heidenhain's lever-thermopile. To study the rapidity of transmission of nerve-force requires considerable apparatus, which it is unnecessary to detail here.

Sensory Nerves.

Here then are two methods. In one you ligate the iliac, then poison the frog and observe if sensibility is increased, diminished, or lost.

Experiment 5.

Frog, femoral artery ligated, poisoned by a subcutaneous injection of 1 c. c. of a watery concentrated solution of atropia. In a few minutes the non-poisoned extremity was half paralyzed, whilst sensibility and motility were preserved in the tied extremity. In ten minutes complete motor paralysis in poisoned extremities. In fifteen minutes irritation of poisoned leg called out no action in the unpoisoned extremity. When the unpoisoned extremity was irritated, there was movement in it. The nerve of poisoned extremity was not irritable, of the unpoisoned extremity like the normal. The muscle of poisoned extremity was less irritable than that of tied extremity. This experiment of Botkin would seem to prove that a large dose of atropia paralyzes sensibility by an action on the sensory nerves. By the preceding method it is very difficult to decide if the ends of the sensory nerves are affected or their ganglia in the spinal cord. The other method is as follows: A frog is poisoned with .001 grain of strychnia, and by its reflex contraction serves as an index of the excitability of a sensory nerve. The sciatic of the frog is bared and dipped into a 2½ per cent. solution of the poison,

and then the irritability is tested; the distance between the spirals being the measure of irritability. The sciatic of the other leg is also prepared in the same manner, and placed on electrodes, whose separation is the same as those on the other sciatic. The bloodvessels of the posterior extremities are ligated. The second sciatic dips into a 2½ per cent. solution of phosphate of soda. Two other pairs of electrodes are placed at similar places on the sciatics, towards their central extremities. Now, when a reflex contraction is the measure of irritability of a sensory nerve, any increase or decrease of it can be discovered.

Experiment 6.

R, right sciatic in 2½ per cent. solution of phosphate of soda.
L, left sciatic in 2½ per cent. solution of sulphate of atropia.
C, central part of nerve.
P, peripheral part of nerve.

The numbers indicate the distance the secondary spiral is separated from the primary. To produce a reflex contraction, the weakest current necessary is taken.

	P.		C.	
Time.	R.	L.	R.	L.
10.55 A.M., ...	9	11	14	21
11 00 A.M., ...	9	15	13	22
11.05 A.M., ...	10	13	13	16
11.10 A.M., ...	12	8	34	16
11.15 A.M., ...	4	3	40	13
11.20 A.M., ...	3	3	34	16
11.25 A.M., ...	5	2	26	16
			13	8

As the result shows, the excitability is quite fluctuating, so that the most that can be said is that the sensory nerves retain their irritability for considerable time in a 2½ per cent. solution of atropia.

SPINAL CORD.

To determine the action of a drug on the spinal cord, such

as atropia, Professor Fraser* employed the following methods, which I abridge.

Experiment 7.

Four-fifths of a grain of sulphate of atropia was injected with eight minims of distilled water into the abdominal cavity of a frog weighing 455 grains. In eight minutes its movements were sluggish, and some weakness occurred in the anterior extremities. In six hours the nerve paralysis was more complete, stimulation did not excite any reflex movement, and even direct galvanic excitation of an exposed sciatic failed to produce any muscular contraction, although the muscles themselves readily contracted. Sixty-eight hours after the dose, a change of position had occurred; the anterior extremities were flexed, and formed an arch-like prop, on which the raised head and thorax were supported. On the fifth day, tetanic attacks supervened, and lasted in all seventeen days.

This experiment demonstrates that atropia in small doses paralyzes and then convulses. To discover the seat of this tetanus, which may be in the muscles, motor nerves, sensory nerves, spinal cord or brain, is the next problem.

The next experiment proves that the tetanus is not muscular in origin.

Experiment 8.

After the ligation of the right sciatic artery and vein, a frog weighing 322 grains received subcutaneously a solution of three-tenths of a grain of sulphate of atropia in four minims of distilled water. On the third day the reflex movements rarely occurred anywhere but in the right posterior extremity. On the same day, at fifty-one hours, the right (non-poisoned) posterior extremity became extended in violent tetanus when stimulation was applied to any portion of

* Some Undescribed Tetanic Symptoms produced by Atropia in Cold-blooded Animals.

the skin, while everywhere else only feeble reflex movements occurred.

On the fourth day stimulation excited general tetanus, which equally affected both posterior extremities.

This experiment shows that the seat of tetanus is neither in muscle nor motor nerves, as the tetanus occurred equally as well in the regions from which the poison was excluded.

Experiment 9.

In a frog the sacrum was excised, exposing the sacral bloodvessels and nerves within the abdomen of a male frog weighing 210 grains. Then a thread was passed below the nerves firmly ligaturing the abdomen, including all its bloodvessels, but excluding the sacral nerves. After the operative procedure he retained apparently normal control over posterior extremities. Three minutes afterwards he received under the skin at the left side of the thorax $\frac{1}{100}$ of a grain of sulphate of atropia, dissolved in four minims of distilled water. On the following day the anterior extremities were flexed inwards, supporting the head and chest, posterior extremities normally flexed. General tetanic convulsions could readily be excited by moderate stimulation of the skin of any region below the ligature (non-poisoned region) as well as above it.

This experiment demonstrates that the tetanus does not arise from irritation of the sensory nerves, as irritation of the unpoisoned sensory nerve-endings easily produces spasms and tetanus, thereby showing that a direct action on the sensory nerves is not required for the production of tetanus. That the origin of the tetanus is not cerebral is proved by the following experiment.

Experiment 10.

A frog weighing 152 grains received subcutaneously $\frac{15}{100}$ of a grain of sulphate of atropia in four minims of distilled water. The stage of paralysis continued until the third day, and on the fourth day tetanus ensued. On the sixth day,

tetanus continuing, at 2.10 P.M. the spinal cord was divided immediately below the brachial enlargement. Now when the posterior extremities were touched tetanus took place only in them; when the anterior extremities were irritated it took place only in them. As the seat of the tetanus is neither in the muscles, motor or sensory nerves, nor in the brain, it must be situated in the spinal cord.

Now, the theory is, that the paralytic and spinal stimulant actions coexist in frogs after the administration of large doses of atropia.

Experiment 11.

Frog weighing 270 grains. The abdominal aorta was ligatured immediately above its bifurcation into the two iliacs. The fifth of a grain of sulphate of atropia was dissolved in four minims of distilled water, and injected under the skin at the right side of the thorax. In one hour great impairment of motility, and in twenty-three hours the anterior extremities were perfectly flaccid, while the posterior were extended with the webs stretched. Touching the head slightly caused a sudden attack of tetanus in the two posterior extremities. It was impossible to excite any movement in the anterior extremities. At twenty-eight hours the state of things was the same. Touching the skin anywhere excited tetanus only in the posterior extremities. The right brachial nerve was exposed and tested by galvanic irritation, but there was no movement in the right anterior extremity except tetanus of the posterior extremities. On the third day the anterior extremities were rigidly flexed, and on stimulating the skin general tetanus ensued.

This experiment proves that the spinal stimulant action would have been marked by the paralytic, if the posterior extremities had not been protected from the direct influence of the poison. He also adduces proof by synthesis, that atropia is a paralyzer and spinal stimulant. He selected strychnia as a typical spinal stimulant, and sulphate of methylstrychnium as one of the simplest paralyzers. It was

found that a salt of strychnia in the dose of about $\frac{1}{45000}$ of the weight of a frog produced violent tetanus lasting for hours. The sulphate of methylstrychnium, varying from $\frac{1}{800}$ to $\frac{1}{15000}$ of the weight of a frog, produced complete motor nerve paralysis without death.

Experiment 12.

One minim of a mixture of two minims of liquor strychnia (B. P.) in eighteen minims of distilled water (equivalent to $\frac{83}{100000}$ of a grain of strychnia), was added to three minims of a solution of one-tenth of a grain of sulphate of methylstrychnium in ten minims of distilled water (equivalent to $\frac{1}{300}$ grain of sulphate of methylstrychnium). Four minims of this solution was subcutaneously injected into a male frog weighing 355 grains. In three minutes the frog was unable to jump, in twelve minutes only feeble reflex movements could be excited, and in thirty-five minutes it was impossible to excite any reflex movement. During all this time there was not the faintest symptom of strychnia. At forty minutes the sciatics were completely paralyzed, and the heart-beat was twenty-eight per minute. Twenty-four hours afterward the anterior extremities were rigidly incurved, and on slight touch tetanus ensued, which state continued for five days when the skin was irritated. On the twelfth day the frog was normal. Here strychnia and methylstrychnium sulphate produce a series of symptoms in every way like those produced by atropia on the cerebro-spinal nervous system of frogs.

Atropia has greater paralyzing power than spinal stimulant power; hence the paralysis preceding masks the spinal stimulant action, till the motor nerves recover from their paralysis, and tetanus supervenes. In warm-blooded animals the paralysis of motor nerves is not so rapid as in frogs; hence you have only partial paralysis, whilst in batrachians complete.

He has illustrated this by means of Fig. 11. Here the

normal line is A B, whose divisions correspond to a period of twenty-four hours. C D represents the line of complete paralysis, and the curve of paralysis is represented by O P P_2, etc., whilst the curve representing the spinal stimulant action is O S_1, etc.,

FIG. 11.

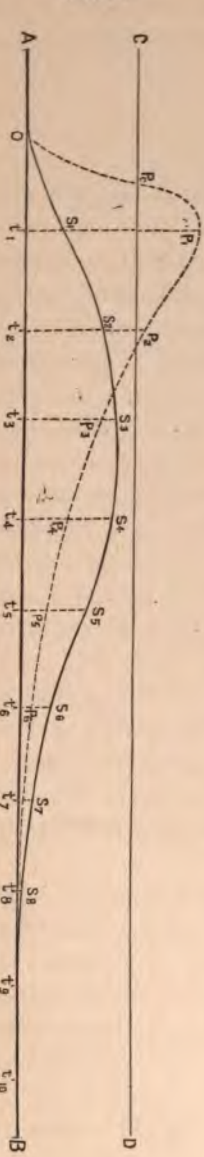
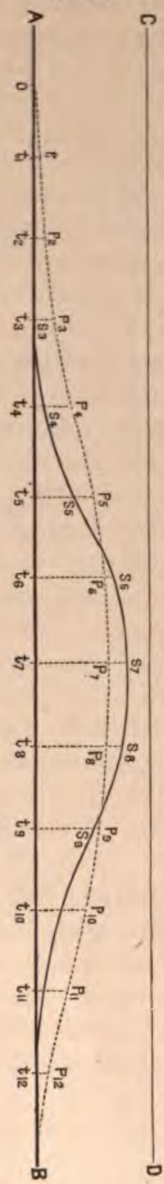


FIG. 12.



The lines t_1 S_1 t_2 S_2, etc., represent roughly the amount of tetanic action, while the lines t_1 P_1 t_2 P_2, etc., represent the amount of paralysis. Now the frog is in a state of paralysis as long as the line of tetanus O S_2, etc., does not cut the line of paralysis, O P_2, etc. When the tetanic action becomes predominant, the paralysis is constantly decreasing. Here during the time represented by O t the spinal stimulation is completely masked by the paralysis existing, the tetanus appearing as the paralysis is vanishing.

The effects of this combined action on a mammal are graphically represented in Fig. 12.

Experiment 13.

The experiment was on a dog weighing fifteen

pounds, which received eight grains of sulphate of atropia in a solution under the skin. Slight paralysis was observed at twenty minutes, and feeble spasms occurred at forty minutes. They together reached their maximum intensities at about seventy minutes, and the spasms ceased at one hundred minutes, while the paralysis continued until about one hundred and twenty minutes. The dog recovered perfectly.

A B, in Fig. 12, represents the normal line whose divisions represent periods of ten minutes. C D is the line of complete paralysis, and the curve of paralysis is represented by the line O P_1 P_2 P_3, etc., whilst the curve of spinal excitation (tetanus) is shown by O S_1 S_2 S_3 S_4 S_5 S_6, etc. The lines t_1 P_1 t_2 P_2 represent the amount of paralysis, whilst the lines t_3 S_3 t_4 S_4, etc., represent the amount of tetanic excitation. Now as the curve of paralysis never reaches the line of complete paralysis, C D, tetanic action is not marked as in frogs, and consequently paralysis and convulsions are seen during the period of poisoning. Hence it is inferred that the action of atropia on the central nervous system is due to the combined spinal stimulant and motor nerve-paralyzing action, and that the different effects in different species of animals are due to this combination acting on special varieties of organization.

Effect on Reflex Action.

To study the effect of a drug on reflex action, the method of Türck is best. You perform the experiments in a room not heated above 15°–16° C., as otherwise the reaction soon ceases and death ensues. A $\frac{1}{5}$ per cent. solution of sulphuric acid is used to dip the foot of the frog in, and after this the foot must be washed off with water, and observations must not be taken too often. To prepare the frog, you cut through with scissors the skull on a line with the posterior edge of the membrana tympani, severing the medulla, avoiding hæmorrhage as much as possible. Then after placing him in a moist chamber for at least half an hour longer, you suspend him by means of Bowditch's wire-holder, and make

observations every ten minutes, till the three observations are the same or nearly so. Then inject the substance and wait fifteen minutes, as the injection irritates the sensory nerves and reduces reflex irritability, and test how long the foot remains in the acid solution. When the foot is dipped into it, it must be immediately immersed into a cup filled with water, to wash off the acid, lest it act too much on the skin.

For a reflex act, the following organs come into action: end of a sensory nerve, the sensory nerve-trunk, the motor nerve-end, the motor nerve, and the muscle and spinal ganglia. To decide that the lowering of reflex action is not dependent on a lessening of the conductivity of a nerve, you poison the frog, and test the irritability from time to time, till all reflex excitability ceases. If now you bare the nerve and find that its irritability is normal by induction currents, then you may assume that it has no action in the depression of reflex excitability.

To decide if the sensory nerve-ends or the spinal cord are affected, you isolate the nerves going to the posterior extremities, put a strong thread under them, draw the ends together, and tying them, you shut off the circulation of blood in the posterior extremities. If now you poison and there is at length no reflex action in the anterior extremities, you test the posterior extremities, and if there is none here, you assume that the drug acts on the spinal cord. Having studied the action on the spinal cord, the action on Setschenow's centres is taken up. Here you sever the cerebrum by a scissors passed through the skull on a line with the anterior edge of the membrana tympani. Then after waiting a few hours, you put the animal in Bowditch's wire-holder, and test the reflex excitability by means of the acid solution already described. Then the poison is injected, and after waiting some minutes, you again test with acid solution every fifteen minutes. When the reflex excitability is considerably depressed, you divide at the medulla, and after waiting some minutes, again test and see if the reflex excitability rises. Should the

drug have depressed the reflex excitability, and on division at the medulla the reflex excitability rise, you may infer that it acted on Setschenow's centres, provided you have already proved that it has no action on the spinal cord. To measure the time, you let a metronome beat a hundred times per minute, and count the beats during which the foot remains in the acid before its withdrawal. Care must be taken that there is not much hæmorrhage, as it acts as an excitant to Setschenow's centres. The decrease of heart-beats must also be observed, as it does the same. Neither hæmorrhage, unless great, nor cardiac paralysis have any very immediate effect on the reflex excitability of the spinal cord alone. In studies on the spinal cord of warm-blooded animals, the quality of the blood, the rapidity of the heart, or size of capillaries are to be observed.

Action on Medulla Oblongata.

When convulsions are cerebral, they probably have their seat in the medulla. Disturbances in the rhythm of the respiratory movements, vomiting, and so on, are usually supposed to be due to an action on the medulla.

Action on Cerebellum.

Want of co-ordination in voluntary movements when not referable to any other known action may have its seat in the cerebellum.

Action on Cerebrum.

The study of the action of a drug on the cerebrum is best made on man. There is usually an exaggeration of the cerebral functions, such as, thought takes place more rapidly, memory is more vivid, the special senses are excited, as hearing is better, delirium even may be present. Care must be taken to see if it is the result of increased arterial tension or hyperæmia of the brain, which is usually shown by a redness of the face and brilliancy of the eyes. This state is usually

followed by diminution of the cerebral functions, as indisposition to thought, sleepiness, and perhaps narcotism and coma.

Syncope is also a sign of cerebral action, but here care must be taken that the circulatory and respiratory changes are not at the bottom of it. Reduction of respiration causes asphyxia, which causes loss of cerebral action by the want of oxygenized blood. Low arterial tension, either through depressed cardiac activity or dilation of the capillaries through the vaso-motor apparatus, may also cause syncope. To examine the state of the cerebral circulation, Hammond's* cephalo-hæmometer is best. It consists of a brass tube, nickel-plated, which is screwed into a hole in the skull previously made by a trephine. It is open at both ends, but into the upper end there is another brass tube whose lower opening is closed by a thin sheet of india-rubber, and the upper opening is closed by a brass cap, into which is fastened a glass tube graduated by a scale. Into this inner tube colored water is placed, and the tube is screwed down till the elastic membrane presses on the dura mater and the colored column of water stands at 0, which is in the middle of the scale. If the quantity of blood in the brain is increased, the column rises; if it is lessened, it falls. The glass tube should be attached to Marey's polygraph, and be allowed to register the changes. Direct observation of the bloodvessels, by inserting a glass plate into the skull, is also a valuable means.

Respiration.

To study the effect on the respiration, the following questions arise: How does atropia act on the vagus-ends in the lungs? How does it act on the excitability of the medulla oblongata? How does it affect the aeration of the blood, and what influence does it have on the respiratory centre?

To determine how it alters the aeration of the blood, poison

* Diseases of Nervous System.

with large doses and observe the color of the blood. When this is done with atropia, the blood is still a bright red. Hence it is inferred that aeration is not much interfered with. To determine its action, you take a rabbit, inject the poison towards the heart, and note the respirations with a polygraph registering them. It is found that they are at first diminished, but afterwards increased beyond normal. Now the question arises, How does this occur? Either the respiratory centres are diminished in irritability, or the vagus-ends are. To decide this, the vagi are cut, and then the rabbit is poisoned. If, now, the paralyzed ends are the cause of a diminution of the respiratory frequency, then it will not occur. When the experiment was made, it was found that no diminution followed, but always an increase of the number of respirations. Hence it is concluded that atropia paralyzes the vagus-ends in the lungs, but later their irritability is restored in a certain degree. A rabbit is taken, and atropia injected into the peripheral end of the carotid; the respirations increase from the beginning, whether the vagi were divided or not. Thence it is inferred that the respiratory centres in the medulla are also excited. To eliminate the effect of psychical agency on the respiratory apparatus, narcotics should be employed. This acceleration of respiration occurs whether the arterial blood-pressure is high or low, so that it cannot be from retarded supply of blood or of oxygen to the respiratory centres.

Action on Superior Laryngeal.

Here you take a cat, inject 1 c. c. of tinct. opii into the jugular, prepare the left superior laryngeal; the abdomen is opened by a longitudinal section. Now irritate the central end of the superior laryngeal, and there is stoppage of respiration in expiration. Now inject .005 gramme atropia, and five minutes afterward irritate the central end of the superior laryngeal nerve, and stoppage in expiration still takes place, showing that atropia has no effect on the reflex inhibitory fibres of the superior laryngeal.

ACTION ON THE PUPIL.

To study the action of a drug on the pupil, internal and local application is made, and the effect observed. To study the effect, a rabbit is bound down, and the under lid is caught by a small bull-dog forceps, which is loaded with a weight. The membrana nictitans is drawn aside by a thread passed through it. The external commissure is also slit up for better observation of the iris. Then the sympathetic along the carotid in the neck is sought, and put on a fine thread to raise it, when it is irritated by an electric current. The oculo-motor is then prepared as follows: artificial respiration being kept up, the top of the skull is removed with a little bone forceps, the carotids being compressed, the cerebral hemispheres in great part removed, and the olfactory bulbs divided The remainder of the cerebrum is raised on a spatula, when the thick white optic nerves are seen, which are also divided. If now the brain is elevated still higher, two thin white nerves are seen, the oculo-motors, which at their central extremity are divided and put on the hook-like electrodes of silver wire. The bleeding can be checked by bovista or pincette. With the sympathetic only prepared, a rabbit received a dose of atropia. Before the instillation of the atropia, the pupil measured five millimetres, afterwards it was ten millimetres, and during irritation of the sympathetic eleven millimetres. This experiment proves that after atropia has dilated the pupil, irritation of the sympathetic will still further enlarge it.

The next experiment is made as follows:

If four electrodes are joined to the secondary spiral of Dubois's induction apparatus, and placed in the shape of a square on the inner edge of the iris, so that diagonal poles correspond to the same electrode of the secondary spiral, the pupil will contract.

In a rabbit with four electrodes arranged as described, the diameter of the pupil was five millimetres before the atropia, and ten after the instillation, and during the electric

irritation seven millimetres. This experiment demonstrated that the pupil still contracts after direct irritation. In the third experiment, a rabbit's oculo-motor nerve was prepared, artificial respiration being kept up, and after the atropia had been given, irritation of the oculo-motor caused no contraction of the pupil as normally takes place.

In the fourth experiment, atropia was given to a rabbit, and two electrodes of the secondary spiral placed on the edge of the cornea. When the current was sent through them, the dilated pupil was still further enlarged.

Now these experiments prove that after the administration of atropia, the sympathetic is still active, that the sphincter pupillæ contracts on electric irritation, that irritation of the oculo-motor is without effect, and that irritation of the dilator pupillæ still further enlarges the pupil; hence it is inferred that the ends of the oculo-motor nerve in the pupil are paralyzed by atropia.

Glandular Action.

As is well known, atropia makes the mouth dry. To prove how this is done, you take a large dog with a long nose. The submaxillary gland is laid bare, and a canula bound in its duct, the chorda tympani sought, prepared on a ligature and cut. Then irritate the peripheral end, and measure the amount of saliva flowing out in a given time, then give by the vein .003 grain of atropia and irritate the chorda, and the canula will remain empty of saliva. Here the chorda is paralyzed, but Heidenhain has shown that the dilator vaso-motor fibres are not, as the bloodvessels dilate and the blood flows more rapidly, being of a bright red color.

Atropia does not affect the action of the sympathetic on the gland.

Action on Intestinal Movement.

Here take two cats similar in size as possible, and by a longitudinal section in the linea alba, open the abdominal

cavity; the splanchnics are then sought, freed, and put on a ligature and divided.

Then one cat is poisoned with .005 gramme of atropia. Both cats are killed, and the intestinal movements watched, when the intestinal peristalsis will be seen to be active in them, but upon irritation of the peripheral end of the splanchnics the movements in the normal cat will come to rest, whilst in the other there will be no change. Hence the inference is that atropia has paralyzed the inhibitory fibres in regard to their action on the intestino-motor ganglia.

CHAPTER III.

ACTION ON CIRCULATORY APPARATUS.

THE heart is a pump, whose object is to supply the living tissues with blood. It is self-supplying and self-acting in its movements, being independent of the will. Its walls, instead of being formed of inorganic materials, like other pumps, are composed of elements called muscles, which, like the voluntary muscles, are striated, thus standing in contrast with the other involuntary muscles. Cardiac muscles anastomose and intertwine in various directions, containing imbedded in them masses of nerve-matter called ganglia. Many of the agents, such as oxygen, temperature, rest, and so on, acting on the voluntary muscles, act similarly on those of the heart. Cardiac muscles have irritability and the power of contraction, like those under the influence of the will. But the irritability of the heart has characteristic peculiarities which distinguish it from voluntary muscles, as faradic currents, which throw a voluntary muscle into tetanus, cause in the case of the heart only an acceleration of its movements.

Professor Bowditch* has discovered the following law about cardiac muscles: The weakest faradic current able to cause the heart to contract does not generate the weakest contraction possible. When the intensity of the current is increased, the extent of the contraction does not exceed an impassable maximum. When you apply an induction current to the ventricle of a frog's heart, it produces either a contraction or does not, and when the contraction takes place, it is at the same time the most extensive contraction

* Ueber den eigenthümlichkeiten der Reizbarkeit welche die Muskel fasern des Herzens zeigen ; Ludwig's Arbeiten.

which the electric current at a given time can produce. The variable properties of the muscular fibres are the origin of the different extents of contraction of the apex of the heart.

The number of the pulsations of the heart depends upon the state of the exciting mechanism situated in the heart itself. The irritability of the muscles and nerves of this organ is not a sufficient reason. It is believed that the ganglia in the heart are divided into two kinds, excito-motor and inhibitory, and upon these depends the cardiac movement. The excito-motor ganglia in themselves generate a force which sets the heart in motion. To make this motion rhythmical, and to prevent the excito-motor ganglia from exhausting themselves, is the office of the inhibitory ganglia. The excito-motor ganglia may be compared to the steam which sets the engine in motion, and the inhibitory ganglia to the governor or flywheel which makes the motion regular. The exciting ganglia in the frog's heart are situated in the dilated end of the inferior vena cava, the sinus venosus in the frog, and in the septum between the left auricle and ventricle, the former being Remak's and the latter Bidder's. The inhibitory ganglia, or Ludwig's, are situated in the intra-auricular septum.

Nerves of the Heart.

The two great nerves influencing the rate of pulsation of the heart are the pneumogastrics and accelerators; the former slowing the heart, the latter making it run faster. The pneumogastrics arise from a centre in the medulla, and pass down the neck, ending in the inhibitory ganglia situated in the heart. It makes no difference whether you irritate the centre of the pneumogastrics, their trunk, or their peripheral end in the heart, the same result follows, that is, a diminution of the number of heart-beats. A tap on the abdomen is able to throw the pneumogastrics into greatly increased action, so much so that the heart is often stopped and death ensues. Here the sensory nerves convey the impression up

the spinal cord to the centre of the pneumogastric in the medulla, which sends an impulse down its nerves which arrests the heart, and always in diastole, never in systole. All the sensory nerves of the body have a reflex relation to the pneumogastrics. Even pinching the skin in some animals is sufficient to stop the heart. If the pneumogastrics are divided in the neck, the heart runs with great rapidity, because the inhibitory power coming from the centre in the medulla is removed; a brake is taken off the heart. If now with an induction apparatus you irritate the peripheral end of the pneumogastric which is in connection with the heart, you will stop this organ. Digitalis, veratria, carbonic acid, and sad news, will slow the heart by acting on the inhibitory ganglia, throwing them into increased activity. Muscarin, an alkaloid obtained from a species of poisonous mushroom, will also stop the heart just as the electric current did, by increasing the inhibitory power of the ganglia at the peripheral end of the pneumogastric. But if you give atropia, and wait some time, you will find that electric irritation of the pneumogastric has no effect on the heart's movements. Here the poison has caused paralysis of the pneumogastric's inhibitory ganglia. Now in a heart stopped by muscarin, when you give atropia this organ will commence to beat again, but when nicotin is given no movement of the heart will take place. Schmiedeberg explains this as follows: Muscarin stops the heart by irritating the inhibitory ganglia, whilst atropia has the power to paralyze the same; hence the increased activity of these ganglia being abolished, the heart under the spur of the excito-motor ganglia again commences to beat. But nicotin like atropia, as has just been stated, paralyzes the pneumogastric. To explain why nicotin does not start the heart stopped by muscarin, Schmiedeberg has assumed that nicotin paralyzes not the inhibitory ganglia like atropia, but an apparatus seated between the endings of the pneumogastrics and the inhibitory ganglia. Many alkaloids paralyze the pneumogastrics, such as aconite alkaloids, conia, and lobelina.

Calabar bean has the power to restore the activity of the pneumogastric when it is paralyzed by atropia.

Accelerators.

The accelerating nerves arise in the medulla or higher and pass down the spinal cord, emerging in the rabbit through the inferior cervical and first dorsal ganglia, corresponding in man to the middle and inferior cervical ganglia, and passing to the heart, probably ending in the excito-motor ganglia. Unlike the pneumogastrics, they are not in constant action. Some accelerating fibres sometimes pass through the cervical sympathetic nerve to the heart. These accelerating nerves are the antagonizing nerves of the pneumogastrics. Ludwig holds that the reduction of blood-pressure in the capillaries of the brain, and especially in those of the medulla, excites them, that muscular action cannot act reflexly on them; the exhilarating emotions and diminished blood-pressure throw them into activity. When the heart beats rapidly from any news which is agreeable, or one feels light at heart, it is due to the influence of the accelerators; oxygen also stimulates them.

Nerves Acting on the Bloodvessels.

The arrangement of the vaso-motor apparatus is, according to Huizinga,* as follows:

I. Ganglia in the walls of the capillaries or about them, regulating their calibre.

II. Spinal vaso-constrictor fibres going to the muscle in the arterial walls.

III. Spinal nerve-fibres inhibiting the peripheral vascular ganglia, vaso-dilator fibres.

IV. Inhibitory fibres from the skin to the vascular ganglia in their vicinity.

Now irritation of the skin can cause a dilatation of the capillaries through the inhibitory fibres, or contraction through the vaso-constrictor fibres.

* Pflüger's Archiv, vol. xi, 207; Bowditch, Boston Med. Jour., July, 1877.

The vaso-constrictor and vaso-dilator nerves emerge from the spinal cord through the spinal nerves. The vaso-constrictor fibres are united with a nerve-centre in the brain called vaso-motor, its extent being in the rabbit within a millimetre of the tubercula quadrigemina in the upper limit, and within four or five millimetres of the calamus scriptorius in its lower limit; the extent from above downward being about four millimetres. From the centre vaso-motor fibres arise and pass down the spinal cord, emerging as follows: For the head instead of passing directly they go through the cervical sympathetic to the bloodvessels of the face, ear, and pia mater; for the upper extremity through the sympathetic and brachial plexus; for the lower extremity through the lowest spinal nerves to the sacral plexus, and in the trunks of the anterior roots of the lowest lumbar and sacral nerves to the sympathetic, and from there to the nerves of the lower extremity; for the cavity of the nose and the greater part of the mouth through the trigeminus; for the abdominal contents through the splanchnics, which are the most important of the vaso-motor nerves. Around every capillary there is a plexus of nerves and ganglia which keep the vessel in a state of tonic contraction; this system of nerves is called the peripheral vaso-motor system. The tonic contraction of the bloodvessels by these ganglia is re-inforced by impulses coming from the vaso-motor centre in the brain through the nerve-fibres; this main vaso-motor centre is in constant action. When a sensory nerve is stimulated this centre is thrown into increased activity, the bloodvessels in general contract, and of course raise the blood-pressure in the arterial system by the increased resistance to the passage of arterial blood into the venous system. Besides the above contraction of the capillaries throughout the body, there is a local action consisting in a vascular congestion of the region to which the irritated sensory nerve is distributed. The mechanism that takes place here is, that the inhibitory fibres from the skin paralyze the peripheral vascular ganglia in the vicinity; but there is a sensory nerve which when excited

does not only inhibit the vaso-motor mechanism in the parts supplied by it, but paralyzes the main vaso-motor centre in the brain, and thus causes the whole capillary system to dilate. This nerve in the rabbit arises by one root from the pneumogastric, and by another from the superior laryngeal. Its mode of termination in the heart is not yet known. When it is divided and its end in connection with the brain is irritated, all the capillaries of the body dilate, chiefly those of the abdominal viscera, and the blood-pressure falls by necessity, because the resistance to the passage of the blood from the arterial system to the venous system is diminished. This nerve is called the depressor of Cyon and Ludwig. It is not in constant action. It is through this nerve that we become conscious of the state of the heart, whether it beats fast or slow, lightly or heavily. The function of this nerve may be compared to that of a safety-valve on a steam-engine, where if the pressure of steam is excessive the valve gives way and allows it to escape. Here, when the heart is surcharged with blood, the impression is carried by the depressor to the vaso-motor centre, which is paralyzed and allows the capillaries to dilate, which removes the pressure, and the heart soon empties itself through the enlarged conduits, and all danger of cardiac rupture is avoided. Besides the vaso-motor centre in the brain, there are vaso-motor centres in the spinal cord which can come into play. Dr. Schlesinger, of Vienna, has found in rabbits that after section of the spinal cord at the atlas the injection of strychnia into the blood-vessels causes a rise of blood-pressure, and that irritation of a sensory nerve causes a still greater rise. Dr. W. H. Klapp and I have seen a similar effect take place in cats. Here the drug strychnia throws the spinal vaso-motor centre into action, which causes the capillaries to contract, and establishes a reflex relation between them and the sensory nerves, which normally does not exist. Certain poisons, like thebain, throw the vaso-motor centre in the brain into increased activity.

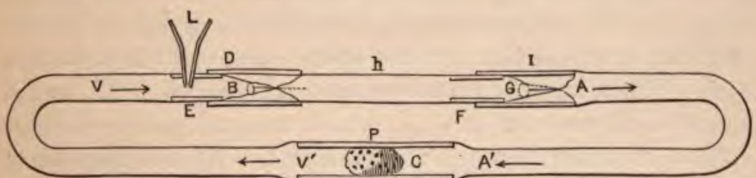
Professor Rutherford has found the depressor in action in three cases.

SCHEMA OF THE CIRCULATION.

Blood-pressure.

When a tube with elastic walls is filled with water, and it receives a blow, a wave movement goes through the contained water. This wave is called a positive wave. Such a wave is also made when the heart contracts and produces what is commonly called the pulse.

If a tube is inserted into water, and it is suddenly sucked full, there is generated a negative wave in the water. Blood-pressure, or tension of arterial system, is dependent on two factors, the contraction of the heart and the unequal pressure between the arterial and venous system produced by the resistance which the capillary system offers. To show this, Weber's schema is best, following in the main its physical explanation as given by Fick.* Two pieces of small



Weber's schema.

intestine, A A′ and V′ V, of similar size, whose ends A′ and V′ are fastened over a glass pipe, P, and whose ends A and V are fastened over two wooden pipes, D and I. E is inserted in the pipe D, and F in the pipe I. F and E are connected through a piece of small intestine, h. In the pipes D and I you find the valves B and G, so that B closes towards V, and G towards h. In the pipe E is the funnel l, which fills the whole apparatus with water. V represents the auricle, h the ventricle, and B corresponds to the auriculo-

* Medicinische Physik.

ventricular valves, G the semilunar valves. By pressing V, part of the fluid goes in the direction V V′, and another part passes into the ventricle, h. Weber compared the function of the auricle to the brushing off of a heaped-up corn measure, the veins opening into the auricle having no valves. If now you compress h, then the valve B closes and all the fluid goes toward A. If A A′ was an inextensible pipe, then the whole column of fluid A A′ V′ V would be moved at the same time. But here A A′ V′ V is extensible, and a quantity of fluid goes into the extensible tube A, and generates a positive wave, which travels towards A′ V′ V. If there was no valve at G, then the water pushed forward by the positive wave would be returned by a negative wave to the same place. But the valve G prevents negative waves, and produces only positive waves. If then h is compressed there is no return of fluid, but the water, on the relaxation of h, can go through the valve B, which causes a negative wave from V to V′. Suppose we put a sponge in at P, now compress h periodically, then the water accumulates in A A′, since by every compression at h more fluid is driven into A A′ than can pass through the sponge C into V′ in the same time. Then there is an increase of pressure in A A′, and a decrease of pressure in V′ V, which unequal pressure causes a flow of water through the sponge C. This difference of pressure depends on the amount of resistance which the sponge offers to the passage of the water, and this depends on the number and size of the pores of this resistance. In the same manner is the blood-pressure in the arterial system regulated; here instead of a sponge you have a system of capillaries, which offers the resistance to the passage of blood into the venous system. If the capillary system is widened the blood-pressure falls, if it is narrowed the blood-pressure rises. If the heart throws more blood into the arterial system, and the capillaries are narrowed, there is a great rise of pressure; if the heart throws less blood into this system, and the capillaries are widened, there is a considerable fall of pressure. Hence blood-pressure is mainly dependent on the

frequency of the heart and the varying width of the capillaries, which are dependent on the activity of the vaso-motor system. After the compression of h, there must be a negative wave from B in the part V V′. On comparison of what takes place in the circulation, we should expect at every ventricular diastole that a negative wave would take place in the venous trunks, but in living animals there is no trace of it. The cause of this is that the auricular contraction takes place at the same time as the diastole of the ventricle. The elastic walls of the auricle keep the blood at the same pressure, although the quantity of blood in the auricle is growing less. When the ventricle contracts, and the auriculo-ventricular valves are closed, then it is expected that an accumulation of blood will take place, but the auricular walls are giving way and no venous retardation occurs.

The object of the action of the auricular muscles is that the current of blood shall not suffer either an acceleration through ventricular diastole or retardation through ventricular systole. The blood-pressure in man is about one hundred and twenty millimetres of mercury. If the blood-pressure in the brain falls, there is syncope, if it increases then there is confusion of the senses, delirium, and coma. Blood-pressure plays a great rôle in apoplexy where the arterial wall is degenerated, and in obstructions and regurgitation in cardiac affections. Increase of blood-pressure makes the heart run faster, decrease of it makes it go slower.

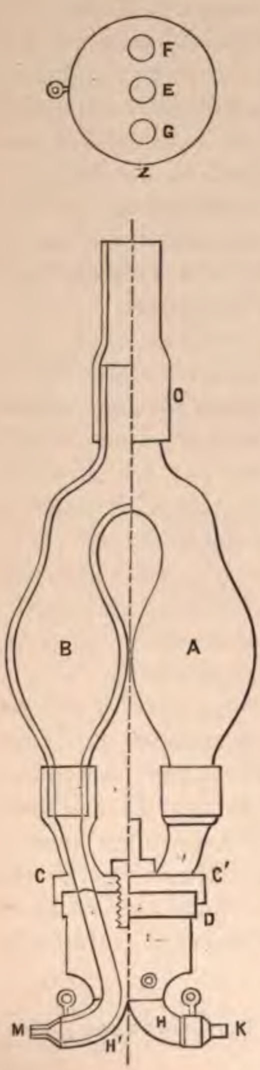
The blood-pressure may be influenced in a reflex manner through the stomach, irritation of the stomach producing fall of blood-pressure. Hering and Breuer have shown that irritation of the peripheral ends of the vagi in the lungs causes the heart to run faster, which I have confirmed.* The rapidity of the heart in glass-blowers is due to this cause, the paralysis of the cardio-inhibitory apparatus, by over-excitation through the endings of the vagi in the lungs.

* Note on Respiratory Apparatus, Journal of Nervous Diseases, 1876.

Rapidity of the Circulation.

To study the action of a drug on the circulation, Ludwig's stromuhr, Fig. 13, is used. It consists of two glass bulbs, A B, united together, and opening into an open tube, O, which is closed by a rubber tube bearing a clamp when the instrument is in use. The other ends of the glass bulbs are surrounded by a metal cap, C, which lies air-tight on a metal plate, D, which, however, allows of rotation. This metal plate, Z, has three openings, the middle one, E, being for the screw to hold the plate to the metal cap, whilst the two openings at the periphery are for two pipes, H H′, which receive the canulas, K M. Now the turning of the metal cap, C, on the metal plate, D, is to the extent of 180°, so that bulbs A B can be put into communication with either K or M canulas. The one bulb, A, is filled with purified olive oil, the other, B, with defibrinated blood. The canula K is inserted in the carotid, towards the heart, and the canula M in the peripheral end of the carotid. Knowing the time it takes for the blood rushing in the canula K to push the oil over into the bulb B from the bulb A, and the capacity of this bulb A being known, and the diameter of the canula, the rapidity of the circulation is easily obtained. Now the

Fig. 13.



moment the oil passes over into the bulb B, by turning the instrument 180°, the blood rushes into B, and pushes the oil back into its original place, the bulb A. Then turning the instrument back 180°, the oil is again forced over into the bulb B. By this means a number of estimates may be made for some time, till coagulation takes place. This is a very beautiful experiment to perform and witness. The defibrinated blood is kept at a temperature of about 40° C., and the oil must contain no air-bubbles, it being introduced by means of a pipette. Several sizes of this apparatus are needed in a laboratory.

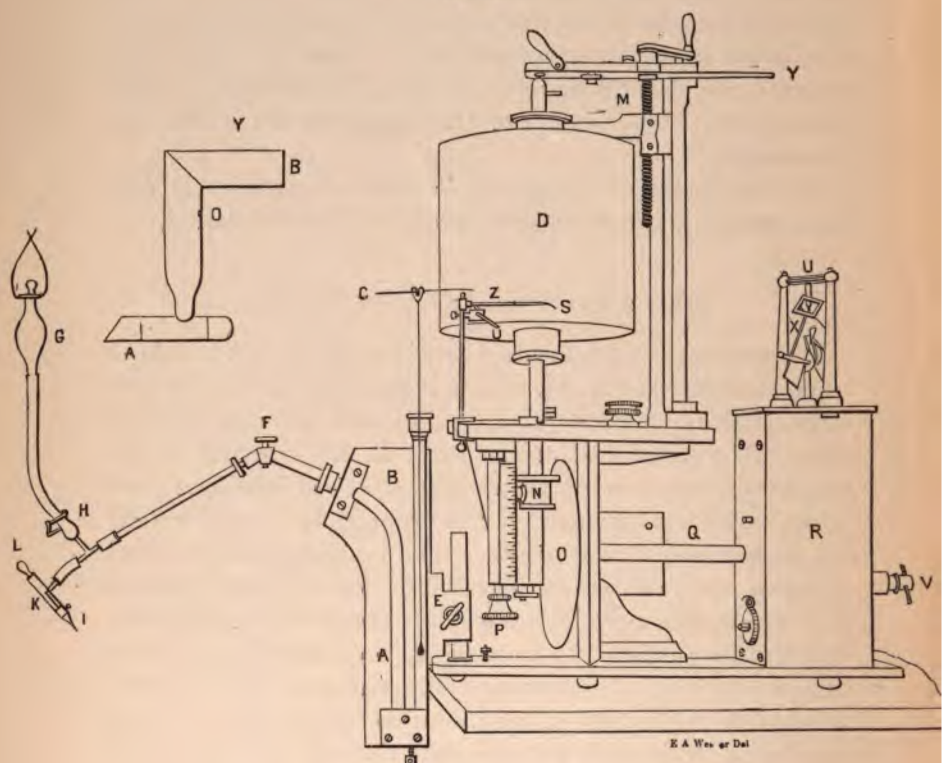
By this instrument Dogiel discovered that alcohol at first increases and then decreases rapidity of the circulation.

Measurement of Arterial Tension.

To measure blood-pressure, Ludwig made use of a U-shaped tube of glass, A, Fig. 14, which is partially filled with mercury, purified by nitric acid, and filtered through chamois skin. The distal end of the tube, B, has floating on the surface of the mercury an upright steel rod bearing a glass pen, C, which is kept against the drum, D, by a small weight suspended on a thread of silk. The U-shaped tube is called a manometer, and can be elevated or depressed by means of a screw arrangement, E. At F is a stopcock, which allows the shutting off of the pressure at any moment, and is a means of filling and cleaning the apparatus. G is a bottle filled with bicarbonate of soda solution, sp. gr. 1026. When the clamp, H, is removed, the soda fills the tube from the canula, I, to the top of the mercury in A. When this is done, no air-bubbles being allowed to remain, the clamp, H, is again applied to the rubber tube coming from the soda bottle. The canula which is bound in the carotid is fitted, as in the figure, on the tube, K, which has a plug, L, that can be removed at pleasure. The tube, K, is divided into two parts by a thin metallic partition running up about half way. Should a clot of blood form in the canula, I, then the

clip is put on the artery, the clamp, H, removed, and the plug, L, withdrawn, when the soda solution, rushing around the partition through the tube, is able to wash out the clot of blood. When this is done, the plug, L, is again replaced,

FIG. 14.



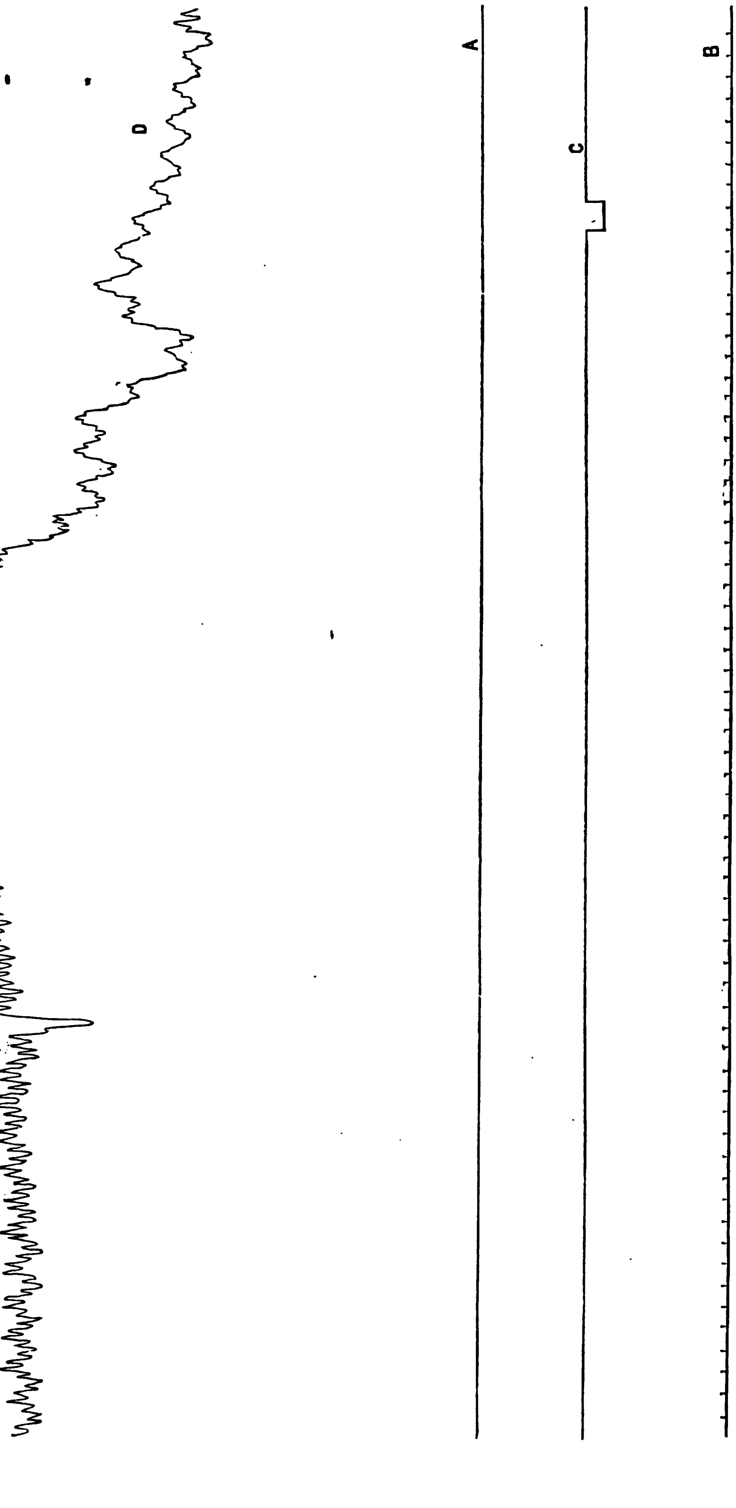
the clamp, H, again applied to the tube, and the clip removed from the artery, when the blood again exerts its force against the mercurial column, elevating the pen, C, at each cardiac beat. Now the revolving drum, D, can be elevated or depressed by the screw, P, when a tracing has been made. The rapidity of the drum is regulated by moving the wheel,

N, from the centre of the circular plate to H, its circumference, by the screw, P. The farther the wheel, N, is from the centre of the plate, O, the more rapidly the drum revolves, the rapidity being made out from the scale opposite, N. The plate, O, is moved by the rod, Q, which is run by clockwork, through the power of a strong spring in the box, R. The movement is rendered uniform by the regulator of Foucault, X. V is a key to wind up the spring, and at U is a drag which catches the spindle and arrests the movement of the apparatus. Y is a movable rod which carries the silk thread bearing a plummet, such as a grain of shot, to keep the pen, C, obliquely against the drum. The drum may be covered with glazed paper smoked by a coal-oil lamp, or it may receive a paper passing in front of it by revolving bobbins. In that case the glass pen, C, must be filled with ink to register the pulsations Z represents Marey's polygraph, to register the respirations. It consists of a metallic cup covered with a thin rubber membrane, which moves a light lever, S, attached to it. Pressure on the air in the cup is communicated by the membrane to the lever, as when you blow into the tube the membrane bulges up and the pen moves.

When the air is sucked out the membrane is depressed, which also pulls the pen down. When a blood-pressure experiment is made the soda bottle, G, is suspended several feet above the apparatus, the clamp, H, loosened, and the soda solution fills the tubes, making the pressure in the manometer nearly equal to that of the animal.

This procedure prevents the blood entering the tube and coagulating, the great difficulty in these experiments; then the clamp, H, is tightened and the clip on the artery is removed, the pulsations being registered on the revolving drum. The point at which the mercury stands before the pressure of anything is put on it should be registered by the pen on the drum, it making a complete revolution. This line is called the abscissa, and is shown in Fig. 15, A. Should a clot form the clip is placed on the artery, stopcock, Fig. 14, F, is closed to keep the mercury at the same

FIG. 15.



height, the plug, L, removed, and the clip loosened a second to allow the blood to drive the clots out of the canula, L; then the soda solution is allowed to traverse the tubing as already described. The pens are made of glass, their points ground obliquely, and if a continuous roll of paper is used, the pen filled with ink has a cotton thread drawn through it, which projects and registers the pulsation.

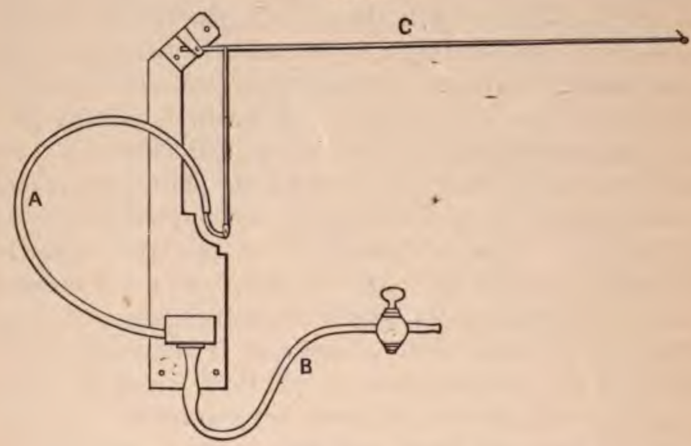
In Fig. 15 is represented a tracing, D, made by Ludwig's kymograph. The line A is the abscissa, the line B contains dots, each one representing a second, and the line C contains a break which represents the beginning and end of the injection of $\frac{1}{10}$th gtt. of lobelina. The smallest curves represent in their ascending limb the systole of the heart, in their descending limb the diastole of the heart. The large curves or waves are due to the influence of the respiration on the blood-pressure. Now by drawing a line at right angles to the abscissa line from the curve at intervals of five seconds or more, determining its length in millimetres and then doubling it, the mean arterial pressure is arrived at. The pressure of the soda solution, sp. gr. 1026, which is about $\frac{1}{27}$th of the whole pressure, is previously subtracted. Having determined the mean arterial pressure before the injection of lobelina, it is immediately determined during and after the injection, for five or fifteen seconds, according to the rapidity of the changes in arterial tension or pulsation. The number of cardiac pulsations and respirations are also counted for fifteen seconds by laying off on the second line, B, vertical lines or ordinates at intervals of fifteen seconds. The pressure and pulsations may be graphically represented on paper ruled in squares. As is seen, lobelina elevates the arterial tension and temporarily slows the heart.

The arterial tension can be estimated by an instrument called the planimeter, but the method already given is sufficiently accurate for researches on the action of medicines.

The mercurial manometer gives neither the absolute arterial tension nor the accurate registration of the systole and diastole of the heart, because the mercury is a heavy body,

which being set in motion is not easily or rapidly brought to rest. Professor Fick, of Würzburg, has made an instrument, Fig. 16, which gives the absolute pressure and a true registration of the movements of the heart. It consists of a C-shaped metallic spring, A, which receives the pressure from the artery through the tube, B. This pressure tends to

FIG. 16.



straighten out the spring, A, which moves the lever, C, upwards and registers the pressure and pulsations on a smoked drum. The spring is filled, before use, with alcohol, and the tubing with soda solution. The tubing may be of lead or of pieces of glass tubing united by rubber corks. The latter means is the one that I used in Fick's laboratory.

ACTION OF ATROPIA ON THE CIRCULATION.

Atropia* in small doses causes an increase of the frequency of the pulse and the mean blood-pressure. With stronger doses the pulse-increase remains and the blood-pressure falls instead of rising, but later again reaches its normal height.

* Von Bezold Untersuch.

If more poison is given there is then a slowing of the heart, which after a few moments becomes accelerated. The blood-pressure sinks very much the moment the poison reaches the heart, then rises again, but finally sinks below normal, and remains there. A decigramme reduces the pulse and the pressure. In dogs the blood-pressure follows the same rules as in rabbits, but the pulse in dogs increases instead of falling as it does in rabbits. From this it is shown that the poison always accelerates the pulse except with large doses on rabbits, and that the blood-pressure is both higher and lower according to the dose. Now the next question arises, are any of these actions due to struggles of the animal? To eliminate these effects experiments were made with woorari, artificial respiration used, and the same results followed. Now, the pulse-rate may be accelerated through increase of aortic tension, through irritation of the accelerator nerves of the heart, through paralysis of the vagus or increased temperature, or through a direct action of the poison on cardio-motor ganglia.

A few minutes after the use of atropia the left vagus was prepared, and the strongest currents applied to it had no effect on the heart. In rabbits the irritability also constantly fell till it was nothing. If now the accelerator nerves or vaso-motor nerves are irritated, they all act except the vagus running to the heart, although the motor and sensory fibres in the vagus act normally. Hence the conclusion, that atropia does not paralyze the trunk of the nerve, but its inhibitory ganglia seated in the heart. The endings of the vagi in the cardiac muscle are greatly different from the termination of motor nerves in striated muscles. They are also different from the ends of the accelerator or sympathetic in unstriped muscle. Woorari in small doses paralyzes the endings of the motor nerves in the voluntary muscles, whilst only large doses affect the terminations of the vagi in the heart. Atropia acts precisely the reverse. Occasionally after irritation of the vagi, when atropia has been used on rabbits, there ensues a rise of blood-pressure.

This has been shown by Rossbach to be due to irritation of the vaso-motor fibres running in the vagi, which cause contraction of the abdominal capillaries, thus elevating the blood-pressure. The next to study is the action of atropia on the vagus roots in the brain. Here the drug is injected into the carotid towards the brain, reaching it before it does the heart.

Action on the Vagi.

To discover if the changes in the heart and circulation are due to paralysis of the vagi, the procedures are as follows: First you can cut the vagi and then see if acceleration takes place: secondly, you can cut the nerve, and test its irritability expressed by slowing the heart by Dubois's coil, then poison, and again test to see if this irritability rises or falls; thirdly, you can study its action on the vagus roots in the brain. To decide, the vagi were cut, the rabbit poisoned by atropia, and the results were that the number of heart-beats were not, especially in dogs, so greatly accelerated as when the vagi are intact. The pulse-rate rather decreased than increased. In fact, poisoning with small doses produced in rabbits and dogs very similar results to those seen when the vagi were cut in those animals. As is seen, the facts suppose a paralysis of the vagi. Now if the vagus is paralyzed, is its origin in the brain, the trunk, or the inhibitory ganglia in the heart the seat of paralysis? The rapidity with which the heart's beat is increased after the poison reaches the heart would incline us to the latter supposition. The next method to study the action of the vagus is to irritate the peripheral end of the vagus. In a dog .0007 gramme of atropia was injected. The pulse rose from 18 to 42 in fifteen minutes. The right vagus was severed and irritated with two Grove cells, the secondary spiral being at 115 millimetres. This irritation decreased the frequency of the heart. Thus a rabbit was taken, heart beating 60 per quarter, when .03

gramme of atropia was injected into the peripheral end of the carotid, the pulse immediately sank to 16, and after a quarter of a minute rose to 66. When the peripheral end was irritated it caused no slowing of the heart. Here there is at first an increase of the inhibitory power of the vagus, followed by paralysis of the vagus. Hence atropia excites the vagus roots in the brain, but the subsequent paralysis of the vagus cuts off this excitation. Should you think that the decrease of blood-pressure was the cause of the increase of heart-beats, you elevate the blood-pressure by compressing the abdominal aorta, either by hand or by tourniquet, or by the injection of defibrinated blood. As yet, there has been but little notice taken of the blood-pressure, which by small doses of the poison causing paralysis of the vagus rises, and with large doses falls. This increase of blood-pressure may be due to either excitation of the cardio-motor ganglia or the vaso-motor centres. Now the arterial tension is dependent on two factors, the strength and frequency of contraction of the heart and the state of the muscles in the arterioles. Then the first question arises, how does the atropia act on the cardio-motor nerves and the cardiac muscle? To decide this, you take a rabbit and divide in the neck the vagi, sympathetics, and depressors, and cut the spinal cord between the atlas and occiput, checking any bleeding by a plug of bovista; artificial respiration is kept up. Now any change must be attributed to the action of the drug on the heart. The experiments showed that the number and strength of the contractions were diminished. The blood-pressure after section of the cord continuously sinks, but atropia makes it sink much faster than it normally does. Now the question arises, what part of the cardio motor apparatus is affected, is it the ganglia, their sensory ends, their motor ends in the muscle, or cardiac muscle itself? These questions are difficult to answer, but the rapidity with which the arterial tension is reduced causes a supposition that it is an intracardiac paralysis of the sensory nerves (which, by the way, are purely hypothetical), preventing the conduction

of an impression to call the heart into action. If immense doses of atropia are injected, the cardiac muscle is not irritable to electric stimulus, hence the muscle is also supposed to be affected. It acts on unstriped muscles somewhat similarly as it does on that of the heart, whilst the striped muscles are not affected. Whilst the changes in cardiac activity partly explain the changes in arterial tension, it is necessary to study how far the vaso-motor nerves and muscles of the arterioles participate in the elevation of blood-pressure. Are the capillaries dilated or contracted?

To decide this, take an albino rabbit, remove the hair from the ear by sulphide of calcium, and watch with a magnifying glass the bloodvessels of the ear before and after the injection. In another rabbit, the muscles of the abdomen will be removed, leaving the peritoneal covering, and watching the capillaries of the intestines before and subsequent to the injection. When these experiments were made, there was no change in the capillaries by small doses, but large doses of atropia dilated them, thus reducing arterial tension. Now the question arises, does it act on the vaso-motor centre in the brain, on the irritability of the trunks of the vaso-motor nerves, or on the irritability of the muscles in the walls of the capillaries?

Vaso-motor Apparatus.

To decide if the vaso-motor centres have been affected, you take a rabbit and inject .005 gramme of atropia toward the brain, when the blood-pressure rises from 98 to 120 millimetres. A second injection of .02 gramme atropia caused a momentary sinking of the arterial pressure. This experiment proves that small doses of this drug, when injected towards the brain, elevate the blood-pressure, and large doses depress it before a considerable portion of the poison is brought into the circulation. Hence the inference is that medium and large doses of atropia reduce the irritability of the vaso-

motor centre. It must not be forgotten that psychical excitement causing convulsions will also elevate the blood-pressure, which is the reason that it is not conclusive that small doses increase the irritability of the vaso-motor centres. To discover if the vaso-motor nerves and the muscles in the arterioles are irritable, the spinal cord is cut, atropia is given, and electric irritation applied to the severed cord, and the pressure will be seen to rise. Large doses, however, destroy the irritability of the muscles in the capillaries to direct and indirect irritation.

Action on the Depressor Nerve.

Here select a cat, and inject $\frac{3}{4}$ c.c. of tinct. opii, and lay bare the left depressor, vagus, and sympathetic. The depressor is surrounded with a ligature, divided, and irritated, when the arterial tension fell. Then .04 gr. of atropia is given, and seven minutes later the depressor was again irritated by electricity, and the blood-pressure fell. In thirty minutes the same result ensued upon irritation. This experiment demonstrates that atropia has no power on the reflex inhibitory action of the depressor.

Some poisons, like calabar, increase the arterial tension by a cramp of the muscles in the walls of the intestines, hence when such a cramp of the intestines ensues, the blood-pressure curve will be taken, and the bared intestine observed at the same time.

To show how a more detailed study of the vaso-motor apparatus may be made, I give one of my pupils' efforts in this direction. Dr. R. M. Smith, in a series of experiments on sanguinarina, found that it produced a fall of pulse and blood-pressure, the fall of the latter being preceded by a temporary rise. In a cat he divided the vagi, gave woorari, employed artificial respiration, and injected sanguinarina. He then irritated the sciatic nerve, and found towards the end of the poisoning that a strong current only elevated the

blood-pressure a few millimetres, whilst normally the rise should be many. Now this want of increase of arterial pressure might be due to a paralysis of the sensory fibres, or of sensory ganglia, no impression being conveyed to the vaso-motor centre. To decide, he gave another cat woorari, screwed Ludwig's gimlet electrodes into the occiput and atlas, and divided in the neck the vagi, sympathetics, and depressors, artificial respiration being kept up, and irritated the vaso-motor centre in a direct manner with an electric current, and found that this caused no elevation of blood-pressure, hence the want of rise was not due to a want of transmission through the sensory communication leading to this centre. Nawalichin (*Centralblatt*, 1870) found that in animals under woorari, and with vagi and sympathetics divided, ligation of both carotids caused a quickened pulse and an increase of 60 per cent. in the arterial tension, this being due to anæmia. Cats were prepared in this manner and sanguinarina given. It was seen that compression of the carotids before the administration of the drug caused a considerable rise of blood-pressure, but when the poison was given that it had no effect. In another cat he divided the vagi, gave woorari, administered sanguinarina, and irritated the depressor, and there was no fall of the arterial pressure, showing, as did the previous experiment, that the main vaso-motor centre was paralyzed to its full extent. To prove that it was not due to paralysis of the vaso-motor fibres, or the muscular fibres in the walls of the arterioles, a rabbit was taken, and the vessels of the ear watched in a favorable light, then sanguinarina was given, the cervical sympathetic divided, and irritated, when the bloodvessels contracted and the pupil dilated to its fullest extent; this completed the train of reasoning that sanguinarina paralyzes the main vaso-motor centre.

In some cases there is a rise of blood-pressure by poisons after section of the spinal cord. Thus, for example, Dr. Schlesinger, on rabbits, and Dr. Klapp,* on cats, have found that

* Heidenhain has confirmed these experiments.

strychnia increases the blood-pressure, and that irritation of the sciatics still further elevates it. The muscular movements were eliminated by the use of woorari. This rise of arterial tension has been assumed to be due to an excitation of vaso-motor centres seated in the spinal cord.

Action on the Accelerator Nerves.

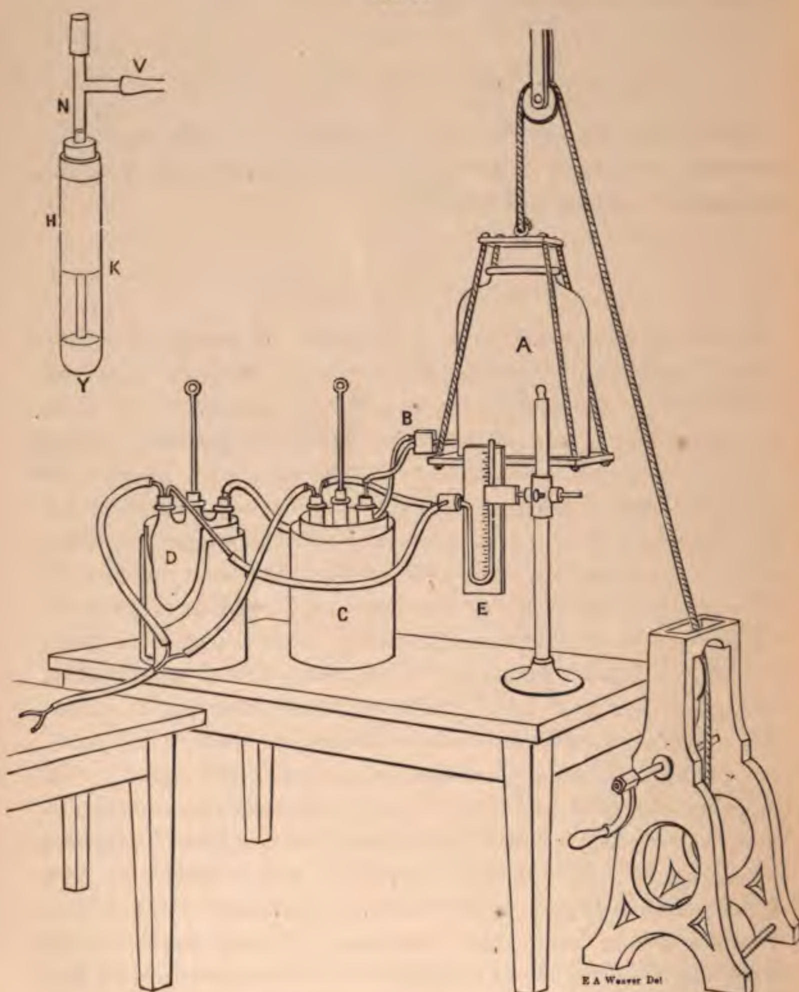
Böhm has shown by his researches on cats that the accelerators are not paralyzed by the action of atropia, although rendered less irritable.

Artificial Circulation.

In studying the action of an organ it is sometimes necessary to establish an artificial circulation of blood deprived of its fibrin. To defibrinate blood, it is allowed to run from the carotid into an open vessel, where it is vigorously beaten by a stick, and afterwards filtered through pure linen. To establish such a circulation, Professor Cyon has constructed an apparatus, Fig. 17. It consists of a large jar, A, filled with quicksilver, which is able to flow out the exit-tube, B, on elevating the flask by the crank and rope arrangement. The exit-tube, B, bifurcates, sending a branch to each flask, C and D. These flasks are filled with blood at different temperatures, and have thermometers inserted in them. They also have exit-tubes which allow the blood to be forced out through them into canulas, which unite and again divide to enter different arteries. E is a mercurial manometer, to show the pressure under which the blood is forced into the bloodvessels. The flasks C and D are inclosed in two double-walled vessels, and between which flows water of the temperature desired in the experiment. Drugs may be mixed with the blood to be circulated, and their action limited to a section of the body, as the brain or heart. To keep the temperature constantly at the same level, there is used an arrangement as shown in Fig. 17, Y. It is Geissler's modifi-

cation of Bunsen's gas-regulator. It consists of a wide tube, H, divided horizontally by a septum, K, which is perforated into two parts; through a perforation in the septum a tube

FIG. 17.



passes nearly to the bottom. The wide tube, H, is stoppered and receives a tube, N, which has a horizontal tube, V,

attached. Inside the tube N, luted to it, runs a smaller tube, which has a small opening opposite the tube V. Mercury is poured into the tube H, and runs down through the perforated partition, K, into the lower chamber of the tube, then the mouth of H is closed and tube N inserted. Rubber tubing is attached to the tube running inside the tube N, and conducts to the gas-reservoir. The rubber tubing attached to the tube V leads to the gas-burner. Here the gas passes down through the tube inside of the tube N, up between its walls and the walls of the tube N, and at V escapes. The tube N and its inside tube are pushed down into the mercury till the mercury closes the lower end of the tube inclosed by the tube N. Now no gas goes to the burner except through the small hole opposite the tube V. The whole is immersed in a water-bath, which must be kept filled with water to a constant level. Heating the tubes makes the flame smaller when the water and the gas regulator become cooler, and the mercury contracts and leaves the mouth of the tube inside N open, and a full head of gas is on till the mercury is again warmed, when the mercury closes the orifice of the tube inclosed by the tube N, and shuts off the gas. By heating with this regulator, a constant temperature, varying only a fraction of a degree for a long time, is obtained.

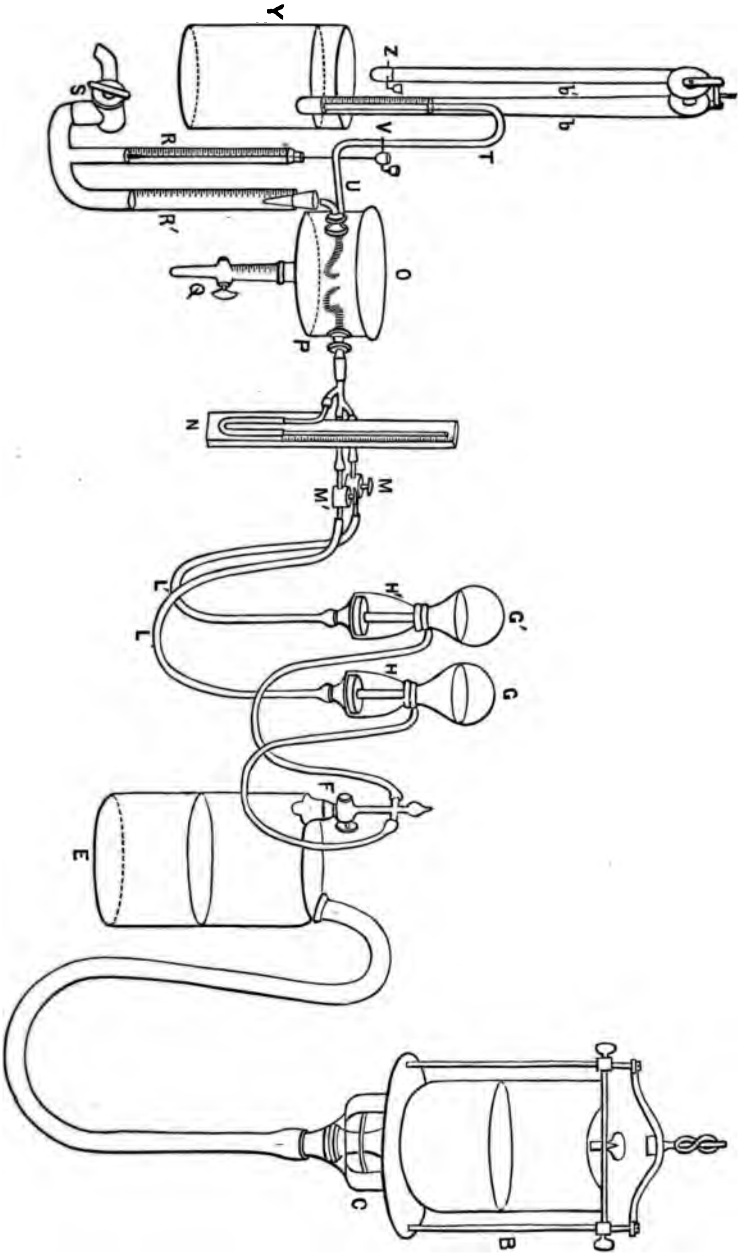
Action of Drugs on the Bloodvessels of Excised Organs.

The play of the vaso-motor centres, the action of the heart, and so on, always come into play in the study of the effect of drugs on the capillaries. To avoid these difficulties Ludwig* and Mosso have carried on an artificial circulation in excised organs, and measured the changes in volume by means of an instrument called the plethysmograph. Fig. 18, B, is a Marriotte flask containing water, which can be

* Ludwig's Arbeiten, 1874.

raised or lowered. The neck of the flask dips into a funnel, C, which communicates by means of rubber tubing with the Marriotte flask, E. The air inclosed in this flask is under the pressure of a column of water, and by means of the stop-cock, F, and rubber tubing communicates with the Marriotte flasks, G G′, which have long necks going into the cylindrical vessels, H H′, and reaching nearly to their bottom. These necks perforate the rubber stoppers in these cylindrical vessels and exclude the atmosphere; these rubber stoppers are also perforated by zinc pipes, which convey the compressed air from the flask, E. Before the flasks, G G′, containing the blood are inverted the rubber tubing, L L′, is attached to the exit-pipes of the cylindrical vessels, H H′. The exit-pipes of the little Marriotte flasks, G G′, are closed by the stopcocks, which open into a tube going to the arterial canula of the prepared organ. The manometer, N, gives the pressure of the blood just before it enters the prepared organ. A flat cylindrical vessel, fifteen centimetres in diameter, over which a glass, O, is slipped is used to receive the excised organ (as, for example, the kidney) on a silk net. The bottom of the vessel opens into a funnel, Q, which communicates with a graduated tube and stopcock. In this way the quantity of exuded material and extravasated blood can be measured. The side of the cylindrical vessel is perforated by three glass tubes, the one marked P carries the blood to the kidney, the second carries the blood flowing out of the vein of the kidney into the manometer-shaped tube, and the third allows the blood at the end of an experiment to flow out through the stopcock, S. To prepare the kidney, a large dog is selected and bled till the anæmic cramps ensue, then the artery is closed and the dog let go. The blood drawn is then defibrinated, to wash out all the clots after death in the renal vessels. Afterwards the dog is again bled so as to exhaust all the blood in him as nearly as possible. When this is accomplished the abdomen is opened (the animal being previously killed by a stab in the medulla), a canula inserted into the renal artery and another in the renal vein.

FIG. 18.



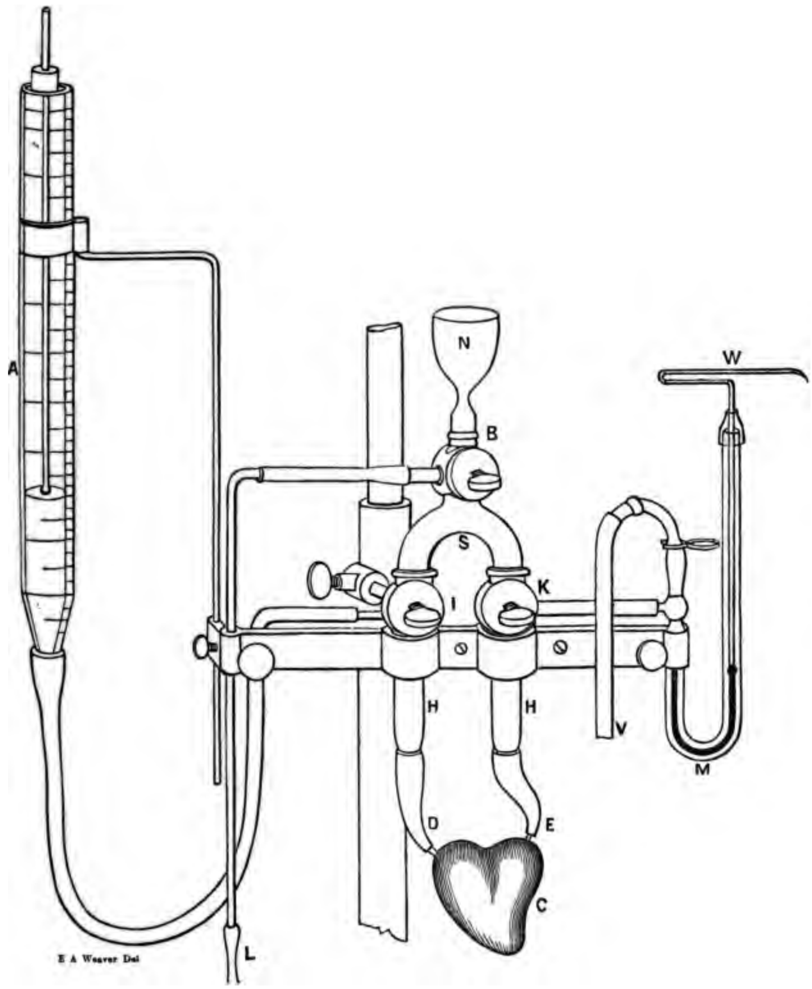
All the little vessels are ligatured, and in a few minutes artificial circulation of defibrinated blood is established, which drives the coagula out of the renal vessels; then the kidney is removed, a ligature thrown around the artery before its division, and a glass canula is inserted; it being previously filled with defibrinated blood by a pipette, excluding air before being joined to the tube in connection with the pressure-flasks. When the apparatus is set in motion the blood does not always begin to flow, seemingly due to a cramp of the bloodvessels, and when it does flow it is uneven because of the contractions. U carries the olive oil which surrounds the kidney to the registering apparatus. The registering apparatus consists of a very thin-walled test-tube, V, about sixteen centimetres in length, which is suspended upon two silk threads, b b′, which run over the double pulley, K. The test-tube is counterbalanced by means of a piece of lead and a glass pen, Z, which registers the changes of volume of the kidney. A large beaker, Y, is filled with oil, on which the test-tube, V, floats, the fluid being on the same level as the venous blood in the exit-pipe. The glass tube, T, conducts from the side opening, U, of the kidney reservoir, P, the oil flowing over into the test-tube, V. In the beginning of an experiment the test-tube, V, is elevated so that it rests on the surface of the oil, and that the vertical limb of the tube, T, reaches nearly to the bottom of the glass. Now when the kidney enlarges, the oil coming over into the test-tube, V, sinks it, and when the kidney shrinks, the oil is sucked up out of the test-tube, V, which moves the pen, Z, registering the rise and fall. The venous blood flowing into the tube, R′, communicates with the tube, R, which contains a float carrying a pen to register the quantity, as this must be measured in every experiment; it is from the arterioles, which are here free from nerve influence. Faradic currents have no effect on the rapidity of the circulation, but galvanic currents increase the rapidity of the current of blood and the size of the kidney; arrest of the current lessens the volume of the kidney. Atropia in doses of $\frac{1}{100000}$ diminished the

rapidity of the flow of blood and the size of the kidney; doses of $\frac{1}{10000}$ did the same, soon followed by increase of rapidity.

THE FROG'S HEART.

To study more minutely the changes in the heart, that of

FIG. 19.



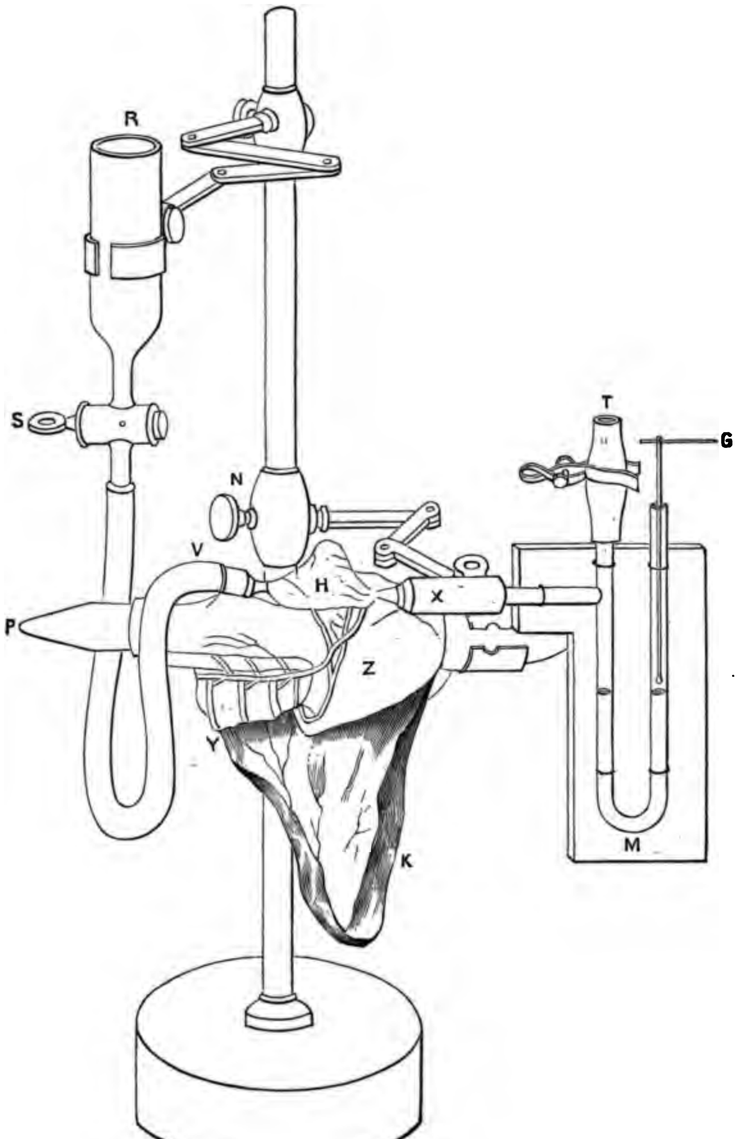
the frog is usually preferred, as the mammalian heart soon dies when excised.

For this purpose the apparatus of Professor Bowditch is the best. It consists, as in Fig. 19, of a Marriotte flask, A, which contains serum and conveys it to the stopcock, I. D is a canula in the vena cava, and E one in the aortic bulb. These canulæ are connected with the glass tubes, H H, which are in communication with the glass stopcocks I and K. K leads to the manometer, and I to the serum-holder. These two stopcocks communicate with a third stopcock, B, also perforated in a T-shaped manner. B leads to the reservoir, N, by which poisons can be introduced to the heart. The tube, L, serves to empty the cup, N, above the stopcock B. The stopcock I allows fresh serum to be introduced at any moment. These stopcocks permit the heart to be washed out at any moment and fresh serum to be supplied.

Every time that the heart, C, contracts, the mercury in the manometer, M, communicates motion to the float bearing the pen, which registers the pulsations on a smoked drum. The tube V allows the manometer-tube to be filled with serum and the air-bubbles excluded. If now a tracing of the heart is taken and some poison added to the serum in the cup, N, and allowed to flow through the heart, the registration will show the changes produced. The heart, C, can be inclosed in an air-tight glass cylinder and be subjected to the influence of gases.

Another apparatus for the study of the changes in the vagus and its ganglia is that of Ludwig and Coats. It consists, as in Fig. 20, of a reservoir, R, with a stopcock, S, which allows the serum to traverse the tubing and enter the heart, H. The tube V is united to a canula in the vena cava, and the tube X is joined to the aortic canula which communicates with the manometer, M. The tube T allows the manometer to be filled without any air-bubbles and is closed by a clip when the apparatus is at work, the pen G registering the movements. N is a screw which allows the apparatus to be elevated or depressed; P is a

FIG. 20.



glass tube over which the œsophagus is stretched; Z is the pneumogastric nerve in connection with the heart, and K is a piece of the skin of the frog to cover the nerve, preventing its desiccation. Y is the vertebral canal. To prepare a frog for this experiment, the cerebro-spinal nerve-centres are destroyed by a wire, the sternum and anterior extremities are removed, and canulæ inserted into the vena cava and aorta. The liver and lungs are separated, leaving, however, a flap of the skin. The œsophagus is then pushed over the glass tube, and the vagus is sought and prepared. The heart should be so filled with serum that pressure on its walls should exist even during the diastole.

In the frog's heart are situated nerve-masses called ganglia, Remak's in the sinus venosus, Bidder's in the left auriculo-ventricular septum, and Ludwig's in the auricular septum. The ganglia which set the heart in motion are called excito-motor, and are comparable to the steam of an engine, the muscles of the heart to the driving-wheels, and Ludwig's or the inhibitory ganglia to the brakes. The inhibitory ganglia are united to the pneumogastrics, and when their trunks are irritated the inhibitory ganglia are set into action and arrest the heart. If now atropia, nicotin, or lobelina are given, the pneumogastrics are paralyzed. When muscarin is given, the heart is arrested by an excitation of the inhibitory ganglia. If now atropia is given, the heart will commence to beat again.

Experiment 1.

8.18 A.M., frog's heart beating 48 per minute, when some muscarin was injected subcutaneously. 8.21 A.M., heart arrested in diastole. 8.24 A.M., two drops of acetate of lobelina subcutaneously. 8.51 A.M., heart remains quiet. 8.52 A.M., .001 gramme of atropia injected subcutaneously. 8.53 A.M., a feeble contraction seen. 8.59 A.M., eight contractions, which, under the administration of .001 gramme of atropia, ran up to forty per minute.

Here atropia is able to start a heart stopped by muscarin, whilst lobelina during seventeen minutes was unable to cause any movement.

Experiment 2.

Frog at 1.30 P.M. received three drops of acetate of lobelina subcutaneously. 5 A.M., heart beat 20; .002 gramme of muscarin into inferior vena cava; heart immediately arrested, and remained so.

This experiment proves that if lobelina is first administered muscarin still stops the heart.

Further, after the administration of lobelina, if the sinus venosus is irritated, diastolic arrest takes place for five seconds.

Experiment 3.

Frog at 1.21 P.M., received three drops of acetate of lobelina. 4 P.M., sinus venosus irritated, and heart stopped for five seconds.

The next question that arises, Does lobelina paralyze the accelerator nerves running in the vagus to the heart, or does it, like nicotin, leave them intact? With that view the next experiment was instituted.

Experiment 4.

Frog at 1.20 P.M., had the vagus bared and carefully put on a thread, when the nerve was irritated with Dubois's coil and one Grove cell at 93 millimetres, when the heart stopped. 1.21 P.M., 3 gtt. of acetate of lobelina subcutaneously. 1.56 P.M., heart-beat 24. 1.59 P.M., heart-beat 24, vagus irritated at 70 millimetres for 15 seconds; Helmholtz's arrangement of the Dubois apparatus. 2.26 P.M., heart-beat 28. 2.27 P.M., heart-beat 28, vagus irritated at zero for 30 seconds.

As is seen, there is no increased rapidity of the heart's action as takes place after nicotin and vagus irritation. Now lobelina paralyzes the pneumogastric, either by paralyzing the inhibitory ganglia or the apparatus of Schmiedeberg

connecting them with the ends of the vagi or the vagi themselves.

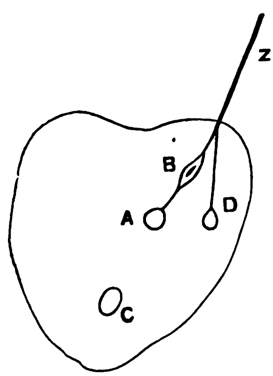
It has been shown by experiment that after muscarin is given, lobelina does not start the heart, but that atropia, which paralyzes the inhibitory ganglia, is able to do so. That after the administration of lobelina, muscarin still arrests the heart, and that irritation of the sinus venosus, the seat of some of the inhibitory ganglia in the heart, causes cardiac arrest. Now as the accelerator fibres in the vagus are paralyzed, the inference is that the inhibitory fibres are also, and that lobelina renders the vagi powerless by paralysis of their fibres, and not through any action on the apparatus of Schmiedeberg. If nicotin is given, the inhibitory action of the vagus is arrested, but the acceleration-fibres remain intact. This is shown in the next experiment.

Experiment 5.

Frog received ½ gtt. nicotin subcutaneously.

4.25 P.M., heart-beat 28. 4.27 P.M., heart-beat 36; the vagus irritated with Dubois's induction apparatus at 130 millimetres. 4.37 P.M., heart-beat 24.

FIG. 21.



Hypothetical arrangement of the nervous mechanism of the heart. C is a cardio-motor ganglion; A is a cardio-inhibitory ganglion; D is a ganglion making the heart run faster; B is the apparatus of Schmiedeberg, acted upon by nicotin; Z is the trunk of the pneumogastric, which sends some accelerating fibres to the ganglion, D.

4.40 P.M., heart-beat 32; vagus irritated with Dubois's induction apparatus at 50 millimetres.

Ligature of the vagus close to the heart, and then irritating the nerve on the distal side of the ligature, caused the heart at 4.45 P.M. to beat 24 per minute.

These facts have led pharmacologists to illustrate the action of the heart as follows: Let Fig. 21 represent a heart. C is an excito-motor ganglion which sets the heart into action, whilst A is an inhibitory ganglion which co-ordinates and arrests the cardiac movements. To this inhibitory ganglion is joined the apparatus of Schmiedeberg, upon which nicotin acts, and in which the vagus-trunk, Z, ends. Conia acts on the trunk of the pneumogastric. The trunk of the vagus also has accelerating fibres, which, when irritated, make the heart run faster, because they go to the ganglion, D, which accelerates the movements of the heart. Want of rhythm in cardiac action is a sign that the excito-motor ganglia are acted upon. To decide if the muscular fibres of the heart are affected, faradic currents are applied directly to the heart, and if the whole heart contracts, the inference is probable that the muscle is not attacked.

If the cardiac muscle only contracts at the part irritated, the probability is that the muscle is affected.

If the striated muscles are attacked, the inference is that probably the poison also injures the cardiac fibres.

CHAPTER IV.

ACTION OF MEDICINES.

TARTAR EMETIC.

Radziejewski, Archiv für Anat., 1871; Ackermann, Virchow's Archiv, bd. xxv, p. 53; Giannuzzi, Centralblatt, 1865, p. 129; Nöbling, Schmidt's Jahrbüch, bd. cxl, p. 24; Richardson, London Lancet, May, 1856; Bucheim u. Eisenmenger, Eckhard's Beiträge, v, 73; Kleimann u. Simonowitch, Pflüger's Archiv, v, 280; Hermann u. Grimm, Pflüger's Archiv, iv, 205; Böcker, Beïträge zur Heilkunde, 11, 234; Parkes, On Urine; Ritter, English Journal of Physiology, November, 1872; Feltz et Barbaran, Robin's Journal, 1875, No. 4; Gähtens, Centralblatt, 1876, No. 18.

Action on Lower Animals.

Tartar emetic causes vomiting, diarrhœa, inflammation of the gastro-intestinal canal, decrease of sensibility by an action on the spinal sensory ganglia, no change in the motor nerves, but in the motor ganglia, great muscular weakness, even before the heart is affected; at first acceleration of the respiratory and cardiac movements, with subsequent decrease of both, fall of blood-pressure, during which the pulse-wave increases. The pulse is sometimes irregular, and towards the end may increase some. Large doses cause death by paralyzing the heart. Its action on the heart is through an influence on the excito-motor ganglia and the muscular structure.

Radziejewski thinks that there is also weakening of the inhibitory ganglia. The fall of blood-pressure is dependent on the weakened force of the heart. The fall of pulse and pressure may be partly explained by the irritation of the nerves in the stomach acting in a reflex manner. It increases the bronchial, salivary, and cutaneous secretions, and lowers

the temperature. The urine is decreased, whilst the urea is increased. It is excreted by the kidneys unchanged.

It deforms the blood-corpuscles, causes the hæmoglobin to crystallize; whilst the albumen and corpuscles are diminished, the fibrin is increased. Fatty degeneration of the liver is produced by small and repeated doses.

On Man.

Here it produces the same symptoms as have been observed in the lower animals. When taken by the stomach it produces vomiting, and if the dose is large, diarrhœa, increase of cutaneous and bronchial secretions, vertigo, roaring in the ears, burning in the mouth and stomach, metallic taste, sensibility of the epigastrium to pressure, acceleration with subsequent decrease of the respiratory and cardiac movements, with an easily compressible pulse and diminution of temperature. The urine contains albumen and antimony. The quantity of carbonic acid exhaled is increased, whilst the amount of urinary secretion is diminished. Larger doses cause great vomiting and purging, insensibility, convulsions, and the collapse of death. Locally, in the shape of a salve, it produces an eruption which resembles that of variola.

Nöbling's theory that the action of tartar emetic on the heart was produced by the potash it contained, and did not take place when soda was substituted for the potash, has been completely disproved by Bucheim and Eisenmenger. Whether this salt produces emesis by an action on the medulla, or by a local action on the stomach, is still a disputed question. Magendie removed the stomach, but still tartar emetic produced vomiting; but Hermann and Grimm have shown that it requires larger doses by the veins to produce emesis than by the stomach, that the first vomiting after the venous injection contains antimony, and that when the stomach is removed the antimony can act on the intestines and pharynx in a reflex manner.

ACTION IN DISEASE.

Tartar emetic is used in mania, delirium tremens, chorea, bronchitis, pneumonia, acute rheumatism, croup, pleuritis, and pericarditis.

In mania and delirium tremens it acts by lowering the blood-pressure, and by a depressant action on the cerebrum itself.

The depression of reflex excitability explains its benefit in chorea.

The increase of bronchial secretion, making it more watery and necessarily more liquid, is one cause of its efficacy in bronchitis.

In croup it facilitates the expulsion of the false membranes by the act of emesis, and possibly by some yet undefined action on the blood, the so-called antiplastic effect.

In pneumonitis the lungs are gorged with blood and exudation, retarding the flow of blood from the right ventricle into the left auricle, the temperature is high, the pulse full and rapid, the respirations frequent. Here antimony reduces the arterial tension, the pulse is slowed, the pulmonic circulation is equalized, the respirations are diminished, diaphoresis is established, and the temperature is abated.

The preceding reasons are sufficient to account for its efficacy in pericarditis and pleuritis.

In hæmorrhages, the diminished rapidity of the heart and the lessened arterial tension are of considerable effect.

As other counter-irritants, it acts by irritating the sensory nerve, producing an afflux of blood to the part supplied by these nerves and a diminished amount of blood to the inflamed part.

When given in divided doses, there soon becomes established a tolerance to larger doses, a fact used in the Rasorian treatment. As an emetic, it is given in small doses, dissolved in a considerable amount of water.

It is contraindicated in cases of much asthenia, and where there is aneurism, hernia, or pregnancy.

VERATRUM VIRIDE.

Bullock, Am. Jour. of Pharmacy, April, 1876; Wormly, Am. Jour. of Pharmacy, Jan. 1876; Bullock, Am. Jour. of Pharmacy, Oct. 1875; Bullock, Am. Jour. of Pharmacy, Sept. 1865; C. L. Mitchell, Am. Jour. of Pharmacy, March, 1874; Peugnet, Med. Record, May, 1872; H. C Wood, Phila. Med. Times, vol. iv; H. C. Wood, Am. Med. Jour., Jan. 1870; Oulmont, On Veratrum Viride; Squarrey, Jour. of Physiology, Nov. 1870.

Veratrum viride contains only two alkaloids, jervia, synonymous with viridia, and veratroidia. Whether veratria is found in this root or not is still *sub judice.*

In the lower animals jervia does not affect the brain or pupil, although Peugnet says it contracts it slightly. It causes muscular weakness, tremblings, clonic convulsions of cerebral origin, no vomiting or purging, profuse salivation, diminished excitability of the motor ganglia of the spinal cord, slowing of the pulse, and decrease of arterial pressure by an action on the muscle of the heart or its contained ganglia and the main vaso-motor centre. The motor nerve and muscles are not affected, and reflex action is greatly depressed through an action on the spinal cord. Peugnet states it is a spinal motor excitant, producing effects similar to those seen after small doses of strychnia.

In lower animals, Wood states that veratroidia reduces the pulse and arterial tension by an action on the inhibitory ganglia, and that large doses paralyze them. It has no effect on the vaso-motor nerves, and kills through the respiratory apparatus.

On Man in Health.

Jervia reduces the pulse without nausea, causes an impression in the throat similar to that occasioned by pyrethrum, numbness of the fauces, languor, but no digestive disturbance. Veratrum viride causes a burning sensation in the mouth, which may reach the throat and cause dryness of the latter, hiccough, malaise, nausea, vomitings which are violent,

tremblings, vertigo, salivation, pulse feeble and slower. In large doses veratrum viride produces great prostration, breathing accompanied with stertor, profuse sweating, vomiting, pulse very weak, apparent unconsciousness, and death.

Unlike veratrum album it seldom produces purging, in which regard it is a superior remedial agent.

Action in Disease.

This medicine is used in fevers, pneumonia, inflammations, neuralgia, and cardiac troubles.

In the inflammations, in typhoid fever, and pneumonia its ability to diminish temperature, to increase the secretions, to reduce the arterial tension and slow the heart are of great value. In the neuralgias the spinal depressant action comes into play.

Where the heart is beating too fast from reflex disturbance, where its action is too violent, as in uncomplicated hypertrophy, this agent would seem to be of considerable value. In aortic constriction, when the hypertrophy has become excessive, it will be indicated.

It does not cause as much muscular relaxation and general depression as antimony.

VERATRIA.

Mossel, Essai sur la Veratrine; Böhm, Die Herzgifte; Von Bezold u. Hirt, Untersuch. aus dem Physiolog. Labor in Würzburg; Fick u. Böhm, Fick's Arbeiten, Zweite Leiferung; Ott, Cocain, Veratria, and Gelseminum; Kölliker, Virchow's Archiv, vol. x; Prevost, Robin's Journal, 1868; Bucheim u. Weyland, Eckhard's Beiträge, v Band.

Action on Lower Animals.

Prevost, in a study on frogs, divided the action as follows: First, a period of excitation, in which there is considerable acceleration of the respiratory movement with a want of voluntary movement. Second, cramplike contractions of the extremities occur, which are not, like those of strychnia,

excited by touch. Third, the cramps pass into a state of resolution, reflex action is decreased, and muscular irritability is lost. It increases the irritability of the motor nerves and muscles, and subsequently reduces it. It probably acts on the sensory nerves at first, exciting and then paralyzing their excitability. It is not decided if it acts on either the spinal motor or sensory ganglia. The convulsions of veratria are mainly due to the heightened muscular excitability, and partly to spinal excitability. When the motor nerve dies it does so from the centre towards the periphery. The muscle curve is greatly changed after the ingestion of veratria. The contraction of the muscle is similar to that observed normally, whilst its relaxation is greatly prolonged. The seat of this prolonged relaxation is in the muscle, and not in the nerve, and is believed to be due to a heightened intensity of the chemical changes going on in the molecules of the muscle.

Small doses of veratria increase the heart-beat, by exciting the excito-motor ganglia of this organ, whilst large doses increase the excitability of the pneumogastric at its cranial origin and at its inhibitory endings in the heart. Then the irritability of the excito-motor ganglia sinks, and thus there is a diminution of the cardiac beats. With large doses the inhibitory power of the pneumogastric is lessened and lost. Veratria prolongs the relaxation of the cardiac muscle like that seen in the voluntary muscle. Death of cardiac muscle precedes that of the voluntary.

The blood-pressure at first increases and then falls. The increase is due to an excitation of the vaso-motor centre, the muscles of bloodvessels, and the cardio-motor ganglia. The fall of pressure is caused by an action of veratria on the endings of the depressor nerve in the heart, which inhibits the vaso-motor centre, and by a subsequent paralysis of it.

Small doses increase the respiratory frequency by peripheral excitation of the pneumogastrics. Large doses reduce the number by a paralysis of the respiratory centres in the medulla.

The blood is less coagulable, and the drug is eliminated by the kidneys. Large doses contract the pupils. The temperature falls after the administration of the medicine.

Action upon Man.

In shape of a salve it excites a feeling of warmth, a burning prickly sensation, redness, and a state of heightened sensibility. Upon the mucous membrane of the nose it causes very great sneezing, flow of tears, burning followed by coryza. When taken internally the taste is sharp, a grating sensation in the throat, burning in the stomach, vomiting, diarrhœa, the stools being bloody, pricking sensation over the body, the pulse and arterial tension are less, the temperature sinks, the respirations are slowed and sometimes increased, the activity of the skin and kidney is greater, with collapse and tremblings.

Action in Disease.

It has been recommended in acute articular rheumatism, pneumonia, dropsy, and neuralgias. Except in the latter disease it has been superseded by veratrum viride and other more appropriate remedies, which cure without the great gastro-intestinal irritation. It is still used considerably in neuralgia in the form of an ointment, where its probable power to diminish sensibility comes into play. As a counter-irritant, in spinal and other affections, it is sometimes used.

ACONITE.

Schroff, Kentniss des Aconit.; Schulz, De Aconitini Effectu; Ott, Physiolog. Act. of Lycoctonia; Murray, M. J., Physiolog. Act of Aconitia and Napellina, Inaugural Prize Thesis, 1876; Hottot, de l'Anatomie et de la Physiologie, 1864, 113; Liegeois et Hottot, Jour. de la Physiolog. 1861, 520; Böhm und Wartmann, Fick's Arbeiten zweite Lieferung; Böhm, Studien über Herzgifte; Weyland, Eckhard's Beiträge, fünf band; Lewin, Rosenthal's Centralblatt, No. 25; Boehm und Ewers, Archiv für Ex. Path., vol. ii, 385; Nunnely, Proceedings of Royal Society, 1869–70; Guillaud, Am. Med. Jour., vol. lxii; Harley, Am. Med. Jour., vol. lxxi; Oulmont, Boston Med. Jour., vol. xciv.

In aconitum napellus there are the alkaloids aconitia and

napellina. Wright states that it also contains picraconitin. In aconitum lycoctonum, there are the alkaloids lycoctonia and acolyctin, the latter being napellina. Wright states that the aconitin of aconitum napellus seems to be wholly dissimilar to the crystallizable alkaloid of aconitum ferox, pseudo aconitin, although the two are doubtless similar in properties. Picraconitin is not identical with Broughton's atisin, obtained from aconitum heterophyllum. Wright inclines to the belief that it is not improbable that lycoctonia and napellina are alteration-products from the action of chemicals on crystallizable aconitia. Physiologically, lycoctonia and napellina are distinguishable from Merck's aconitia by having little or no action on the heart of the frog, whilst affecting profoundly the nervous system.

Action on Lower Animals.

Aconitia in frogs causes fibrillary contractions of the abdominal muscles, which gradually extend to all the muscles of the body, respiration is interfered with, and paralysis ensues without previous general convulsions.

Hottot and Liegeois believe that aconitia first kills the sensory centres, second, the peripheral ends of the sensory nerves, third, the sensory nerve-trunks, and the motor ganglia, but not the motor nerves.

According to Boehm and Wartmann, it either kills or does not the motor nerves, depending on the frog, decreases the reflex excitability of the spinal sensory ganglia, which is the cause of the total paralysis of all voluntary and reflex movements; the reflex excitability is reduced through a spinal action. Guillaud states that there are three periods in aconite-poisoning, contraction, resolution, and muscular death, that it always causes convulsions, that it essentially acts on the spinal and medullary centres, first augmenting, like strychnia, their excito-motor functions, and then paralyzing them. It paralyzes successively the sensory and motor nerves and muscles. In the brain the centres of vol-

untary movement are much enfeebled, but the sensory centres are intact.

One of my pupils, Dr. J. M. Murray, in a very extended series of experiments with aconitia of Merck and napellina of Trommsdorff, found that aconitia, as a rule, paralyzed the motor nerves, that it paralyzed first the ends of sensory nerves, then their trunks and spinal sensory ganglia, and did not act on striated muscles.

Weyland stated that aconitia prolonged muscular contraction like veratria, but neither Boehm and Wartmann nor Dr. Murray could obtain a similar result. According to Dr. Murray, napellina acted very much like aconitia, but the former did not affect the frog's heart and seemed more poisonous than aconitia in equal doses.

In frogs it accelerates the heart for a moment but soon slows it, making its action irregular and finally arresting it in diastole. In rabbits and cats the heart is slowed, while the arterial tension sinks after a previous dose, which does not take place in dogs. The heart runs very rapidly near death. How aconitia acts on the heart is still undecided. Ascharumow thought that it reduced the pulse by an action on the cranial inhibitory centre, but Boehm, Wartmann, and Murray have seen no such result. It paralyzes the pneumogastric and finally the vaso-motor centre in the brain, both to direct and indirect irritation. Aconitia, napellina, and lycoctonia, all produce a delirium cordis, that is, the heart beats slow and fast, the arterial tension rises and falls without any possibility of prediction. After death the cardiac muscle is electrically unirritable In the intravenous injections towards the heart, there is at first a pause in respiration, then violent movements of the chest, after which the breathing becomes regular and reduced in freqnency by an action on the centres of respiration.

After death the blood is fluid.

On Man.

When swallowed it produces a peculiar prickling feeling in the tongue and generally in the mouth and throat, determination of blood to the head, tension and peculiar pain in the temporal region, headache, pain in the epigastric region, sometimes vomiting, decrease of temperature and diminishing sensibility, which begins with formication in the tips of the fingers and toes, ending with insensibility. It causes in the whole region of the trigeminus a peculiar pain, which at first is vague but at length becomes constant. Sometimes stupidity and widening of the pupil occurs. Later there ensues loss of power to see and speak, trembling, vertigo, weakness of legs, respiration is laborious, and asphyxia may result. The pulse which in the beginning was increased sinks to between forty-five and fifty per minute. It is small, weak, and irregular. The face is pale, clammy sweats ensue, and there is great anxiety. Consciousness remains without the least disposition to sleep, but there is at times light delirium After a few gasping respirations and great prostration death follows, sometimes with convulsions. The urinary secretion is increased.

Action in Disease.

It is employed in neuralgia, tetanus, rheumatism, cardiac hypertrophy, aortic aneurism, and fevers.

In neuralgia, especially trigeminal, it probably acts by benumbing the peripheral ends of the sensory nerve.

The reduction of temperature, diaphoresis, and diminution of arterial tension and pulse explain its efficacy in fevers and rheumatism.

When there is cardiac hypertrophy and the heart is acting violently and forcibly, causing disturbance in the circulation, aconite acts by slowing it and reducing its force and the arterial tension.

In aortic aneurism its power to reduce the cardiac force and arterial tension is of great importance.

It acts in tetanus by diminution of the reflex excitability of the spinal cord.

Dr. Fothergill first noticed that the heart of a frog stopped by aconite can be made to beat again by the administration of digitalis.

Dr. Murray, who experimented on cats, found that after the administration of digitalis you can administer ten times the lethal dose of aconite, and then you are unable to completely arrest the heart. Digitalis should undoubtedly rank high among the antidotes in aconite poisoning.

DIGITALIS.

Traube, Gessammelte Beiträge, 1871; Vulpian, Comp. Rendus, 1855; Dickenson, Medico-Chirurgical Transact., 1856; Winogradoff, Virchow's Archiv, bd. 22, p. 457; Ackermann, Deutsche Klinik, elfter bd., 1873; Boldt, Schmidt's Jahrbücher, 1872, p. 29; Meyer, Untersuch., aus dem Physiol. Labor. in Zürich, 1869; Fothergill, Digitalis; Brunton, On Digitalis, 1868; Meyer and Brunton; Journal of Anatomy and Physiology, vii, 153; Stannius, Archiv f. Physiolog. Heilkunde, x, 177; Stannius, Archiv von Reil und Autenreith, xii, 156; Blasius, Fick's Arbeiten, Erste Lieferung; Nasse, Beiträge zur Physiologie der Darmbewegung, 1866; Meihuizen, Pflüger's Archiv, vii, 201; Weil, Archiv f. Anat. und Physiologie, 1871, 252; Lorrain, Journal de l'Anatomie et Physiologie, 1870; Von Bezold, Ueber die Innervation des Herzens; W. A. Hammond, Physiolog. Memoirs; Heidenhain, Pflüger Archiv, v, 40–47; Schmiedeberg, Beiträge zur Anatomie u. Physiologie als Festgabe Carl Ludwig; Binz, London Practitioner, April, 1876; Otto, Centralblatt, 1876, No. 1; Köhnhorn, Bost. Med. Jour., July, 1876; Grützner, Pflüger's Archiv, 1875, heft 6 und 7; Brunton and Power, Centralblatt, 1874, p. 498; Görz, Dragendorff's Jahresbericht, 1873, 562.

This drug contains the following substances, according to Schmiedeberg: Digitonin, a substance very much like saponin, which has been so ably worked up by Köhler; digitalin, insoluble in water and the active element of "Homolle's digitalin;" digitalin, easily soluble in water, the chief element of German digitalin; digitoxin, the most active element of digitalis; it forms a great part of Nativelle's digitalin. Koppe has shown that digitoxin, digitalin, and digitalein are qualitatively alike in physiological action, but that digitoxin is the most energetic.

Action on Lower Animals.

It slows and finally stops the frog's heart in diastole, the retardation being sometimes preceded by an acceleration.

In rabbits, cats, and dogs it produces during the first stage diminished pulse-rate with an elevation of arterial tension, during the second stage lowering of pulse and blood-pressure, and during the third stage the pulse-frequency is very great, with a very low pressure in the arterial system.

The diminution of the number of beats of the heart is caused by a central and peripheral excitation of the cardio-inhibitory apparatus, whilst the subsequent paralysis of the same explains the great cardiac frequency. The fall of pressure is due to lessened number of the contractions of the heart, there being less blood thrown into the arterial system. The cause of the increase of blood-pressure is still *sub judice.* After section of the cervical portion of the spinal cord, Traube and Böhm saw no rise of pressure. Boldt, when experimenting with frogs, saw the bloodvessels contract and subsequently dilate.

Ackermann saw a rise of arterial tension after section of the cord.

Digitalis in medium doses increases the activity of the inhibitory and excito-motor apparatus of the heart, and produces contraction of the capillaries, probably through excitation of the vaso-motor centre in the brain.

Digitalin increases at first the muscular contractions of the heart, which contraction is prolonged as in the tetanic state, and at last it becomes rigid. This happens with large doses in frogs.

It increases the flow of saliva by central excitation of the chorda tympani, which it does not paralyze.

The whole intestinal tract is thrown into a state of contraction by it according to Nasse. It reduces the reflex excitability by calling into increased activity Setschenow's centre. Large doses, when introduced by the vein in warm-blooded animals, cause convulsions by the cardiac paralysis.

The relation between the activity of the heart and the nervous system in warm-blooded animals is much closer than in cold-blooded animals, where we have no convulsions.

According to Ackermann, it increases the temperature externally and diminishes it internally. It acts as a diuretic by producing alteration in arterial tension. There is no direct action on the kidney's structure. It prolongs muscular contraction.

On Man.

Digitalis produces two kinds of effects. In one there is increased salivary secretion, vomiting, colic, and diarrhœa; in the other hallucination, dryness of the mouth, nausea, dilatation of the pupil, vertigo, headache, disorder of vision, objects seeming colored, and mainly in both cases great irregularity of the heart. The pulse is at first slow, then faster, the acceleration sometimes being previous to the retardation. Sphygmographic studies show increased arterial tension. The quantity of urine is increased, the urea, chlorides and earthy phosphates diminished. It acts as an antaphrodisiac by depressing the centres of erection in the spine discovered by Goltz.

Action in Disease.

Digitalis is used in the following diseases: dilatation and hypertrophy of the heart, valvular disease of and palpitation of the heart, in delirium tremens, to promote secretion of kidneys, and in fevers as an antiphlogistic.

In dilatation of the heart it is especially suitable, acting here as a tonic, that is, causing the heart to contract more completely, and thus establishing a greater nutritional interchange of products between the tissues and the blood flowing through them.

In hypertrophy of the heart without valvular disease, the cardiac contractions are sufficient to expel the contents of the heart without any aid of digitalis, in fact digitalis would be contraindicated.

In valvular disease, certainly digitalis has no effect on the lesion. Here it can only act by the effect on the muscular walls. When the heart commences to hypertrophy from valvular trouble, digitalis reinforces the contractile power and enables it to overcome the obstruction and establish a rhythmical and uniform action of that organ. Hypertrophy and dilatation are the results of valvular disease, and the prognosis depends greatly on which takes place.

In mitral obstruction the blood regurgitates into the pulmonary veins, the lungs become gorged with blood, aeration is imperfect, which causes dyspnœa. This obstruction causes the right ventricle to have commencing hypertrophy of its walls. If now the tricuspid becomes affected, then the veins are involved and dropsy results. Here digitalis does good by increasing the contractile power of the right ventricle.

In mitral obstruction the weight, like in mitral regurgitation, hangs on the right ventricle; to that end we give digitalis to increase its driving contractile force.

In aortic obstruction we get naturally a commencing hypertrophy of the left ventricle. Digitalis acts by increasing the force of contraction of the left ventricle.

In aortic regurgitations, on the diastole, the blood flows back from the aorta and through the mitral valve. Here there is an increase of distension and necessity of increased and sustained contractile power, which causes enlargement and thickening of the ventricle. But the aorta is liable in this disease to undergo inflammatory changes which weaken the arterial coats. Hence in increasing by digitalis the already strong ventricular contraction, you run risk of rupturing the aortic coats. Here digitalis is not used, as a rule.

In disease of the right side of the heart digitalis is of no avail.

In fatty degeneration of the heart the digitalis would increase the contractile force of the heart, but the contraction of the capillaries would be antagonistic to this force. In

each case it must be decided whether the increase of contractile force of the heart counterbalances the increased resistance by capillary contraction induced by digitalis. Digitalis should always be used in these cases with great circumspection.

In shock the drug undoubtedly acts by strengthening the heart, and necessarily the other functions of the nervous system dependent on it.

As an antipyretic it is used to lower the temperature. Binz explains this action as follows: The elevation of arterial tension drives the blood from the hot interior of the body to the cooler skin. By increasing the rapidity of the blood, it comes oftener in a given time in contact with the ambient air in the lungs and skin, and thus the body becomes cooler.

In palpitations this drug is especially useful, by making the heart's action rhythmical through its action on the cardio-inhibitory apparatus.

The increase of the arterial tension by this drug makes it dangerous where atheroma of the arteries exists, lest rupture of the arteries in the brain or elsewhere takes place.

Digitalis acts as a diuretic by the elevation of blood-pressure. It has no direct action on the glandular structure of the kidney.

AMMONIA.

Böhm und Lange, Archiv f. Ex. Path., 1874, p. 364; Preyer, Die Blutkrystalle; Koschaloff und Bogomoloff, Rosenthal's Centralblatt, 1868; Bence Jones, Philosophical Transactions, 1851; Funke, Pflüger's Archiv, bd. ix, p. 426; Eulenberg, Die Lehre von dem schädlichen und giftigen Gasen; Feltz et Ritter, Journal de l'Anatomie et de la Physiologie, 1874; Billroth, Archiv f. Klin. Chirurgie, bd. vi, p. 421.

ACTION ON LOWER ANIMALS.

The salts all act alike, although not in the same degree. They produce convulsions of all the voluntary muscles which are spinal. Large doses cause death through spasms. Im-

mediately succeeding an injection into the veins there is a stoppage of the respiratory movements, lasting for a few seconds, and with moderate doses a great rapidity of the respiratory movements without previous arrest. Large doses slow and then increase the number of respirations. The arterial tension, after sinking, temporarily rises, then gradually falls, and soon is below normal. The cause of the low pressure is not through any action on the vaso-motor centre in the brain. The pulsations follow the blood-pressure, rising with it to a certain degree. There is no acceleration of the pulse after section of the cord, which makes it possible that the drug throws the accelerators into action. Feltz and Ritter found that the blood of the dog poisoned by ammonia was deficient in the usual amount of oxygen, and that it refused to absorb it. They observed none in the breath, and Lange thinks that possibly with carbonic acid it forms urea. Increasing the dose of this drug causes a fall of arterial tension to the abscissa, with stoppage of the heart. The irritation of the endings of the vagi in the lungs by it arrests the respiratory movements. Bence Jones found that ammonia increased the acidity of the urine, and thought that it was excreted in the form of nitric acid.

On Man.

When inhaled it irritates the nasal mucous membrane, increases secretion of tears, causes by reflex action, closure of the glottis, cough, and difficulty of breathing. If continued, suffocation takes place or inflammation of the respiratory passages. The pulse may be small, irregular, and accelerated.

When taken internally there is burning in the throat, a peculiar feeling in the head, warmth in the stomach, pulse more frequent and stronger, increase of urinary and cutaneous secretion. Large quantities cause an inflammation of the digestive tract, vomiting, diarrhœa, dyspnœa, cramps, and death, with stupor.

ACTION IN DISEASE.

This drug is used as vesicant or irritant in shape of a liniment, as a stimulant in asthenic fevers, in alcoholic and chloroform-narcosis.

In fevers the sustaining of the circulation is the main point in relief.

In narcosis its stimulant powers set the respiratory apparatus into motion, and excite the brain and nerves.

In bites of insects it neutralizes the poison.

It has been used in snake-bites, but beyond the stimulation of the circulatory and nervous systems it has had no great effect.

ALCOHOL.

Riegel, Deutsches Archiv für Klin. Med., 1873; Brunton, Practitioner, 1876; Bence Jones, Philosophical Transactions; Dupré, Practitioner, vol. x; Richardson, Med. Times and Gazette, vol. 2; Subbotin, Schmidt's Jahrbücher, 1872, bd. cliv; Riegel, Deutsche Klinik, bd. 12, 1873; Binz, Virchow's Archiv, No. 51, p. 153; Binz-Mainzer, Virchow's Archiv, No. 53, p. 529; Runge, Virchow's Archiv, No. 49, p. 265; Davis, Transact. of Am. Med. Associat., 1855; Lussana and Albertoni, Lo Sperimentale, tome xxiv; Bouvier, Pflüger's Archiv, 11, 370; Obernier, Pflüger's Archiv, 11, 494; Brown-Séquard, Journal de la Physiologie, 1859, p. 467; Anstie, Stimulants and Narcotics; Böcker, Beiträge zur Heilkunde; Hammond, Physiological Memoirs; Ford, New York Med. Journal, Jan. 1872; Dogiel, Pflüger's Archiv, bd. viii, 1874; Binz, Practitioner, May, 1876; Binz, Centralblatt, 1875, p. 371; Schmidt, Centralblatt, 1875, 371; Heubach, Centralblatt, 1875, 687; Lewin, Centralblatt, 1874.

ACTION ON LOWER ANIMALS.

In the frog it causes restlessness, the respiration and heart-beat are accelerated, then slowed, the reflex excitability is lessened by an action on the nerve-centres, followed by heightened reflex excitability, and finally complete insensibility to external agents occurs with arrest of the heart; the muscles and nerves preserve their irritability. In warm-blooded animals it produces a state of excitement, with muscular prostration, abolition of intelligence, and immobility to ex-

ternal agents. In dogs after recovery, there is stupidity and timidity, with incomplete paralysis of the posterior extremities, their arterial tension being at first elevated, and then reduced. The vaso-motor centre during the reduction of pressure is inexcitable, which would lead to the conclusion that the elevation of arterial tension was due to its stimulation; the heart-beat is increased,then decreased, and finally augmented. One of my pupils, Dr. R. M. Smith, injected a drachm of alcohol diluted into the jugular of cats towards the heart; here the pulse rose greatly, and remained above normal, whilst the blood-pressure fell during the first minute, rose greatly during the next, and in five minutes fell below normal, and remained there. It increases urinary and salivary secretion.

On Man.

It excites first the cerebrum, then the cerebellum, then the medulla spinalis, finally the medulla oblongata, afterwards depressing their functions.

During the stage of excitement, the brain is hyperæmic, whilst in the depression there is anæmia.

It reduces the temperature, preceded at times by a slight rise. On persons used to the drug, it exerts hardly any effect on the heat of the body. When pure alcohol is ingested, it leaves no taint to the breath, which if observed is due to fusel oil or the ethers. It is mainly oxidized in the body, forming finally carbonic acid and water, which products are excreted by the lungs. It may be excreted as alcohol by the kidneys and skin. It reduces the amount of urea in the renal excretion, and the carbonic acid given off by the lungs. Dr. Hammond has shown that on a diet through which he lost weight, when alcohol was added he gained weight. This fact, taken in connection with the oxidation of this substance in the body, like other foods, cause it to be a true food. During its combustion, it, like other foods, gives off heat. Binz states that one cubic centimetre of alcohol,

during its combustion, gives off enough heat to elevate the temperature of seven litres of water 1° C.

Action in Disease.

This drug is used in asthenic and eruptive fevers, shock, pneumonia, tuberculosis, delirium tremens, dyspepsia, and as a general sustaining agent in prostration of any kind.

In fevers it acts by its stimulant action on the nerves and circulatory apparatus, with the reduction of temperature, and serving as a nutrient.

In shock it arouses the half-paralyzed nerves into action, either by a direct action on the nerves, or by increased cardiac activity. In tuberculosis its nutrient and stimulant qualities come into play. In dyspepsias it stimulates the stomach, in neuralgias alleviates by its anæsthetic property, and in chronic diseases it acts mainly as a concentrated food.

STRYCHNIA.

Heineman, Archiv f. Path. Anat., bd. xxxiii; Mayer, Wiener Med. Jahrbüch., 1871; Nasse, Beiträge zur Darmbewegungen; Cloetta, Virchow's Archiv, xxxv, 369; Kunde, Virchow's Archiv, xviii, 357; Uspensky, Dubois's Archiv, 1865, p. 522; W. H. Klapp, Inaugural Prize Thesis, University of Pennsylvania, 1876; Richter, Zeitschrift f. Rat. Med., 3, xviii; Rossbach und Jochelson, Pharmacolog. Untersuch; Filehne, Dubois's Archiv, 1873, Nos. 3 and 4; Bernard, Leçons sur les Substances Toxiques; Vulpian, Archives de Physiologie, 1870; Steiner, Dubois's Archiv, 1874, No. 4; Ebner, Virchow-Hish's Jahresbericht, 1870, 363; Schiff, Pflüger's Archiv, 1871, p. 229; Bucheim, Pflüger's Archiv; Falk, Dragendorff's Jahresbericht, 1874, p. 489; Gorochofzeff, Dragendorff's Jahresbericht, 1874, p. 489; Heidenhain, Pflüger's Archiv, 1876.

On Lower Animals.

It increases the reflex excitability of the gray matter of the spinal cord, and produces convulsions of a spinal origin. Artificial respiration, by producing apnœa, is able to prevent or palliate the convulsions of strychnia. It does not paralyze the motor nerves. The cause of death in frogs is exhaustion of the excitability of the spinal cord, in warm-blooded animals

asphyxia. In the frog the convulsions are brought out by the least irritation of sensory nerves, and there is a series of convulsive tremblings of all the muscles of the body. If the convulsions are frequent, the spinal cord is exhausted, and the animal loses all reflex action. In warm-blooded animals the convulsions occur spontaneously, but can be excited by touch.

In frogs the heart is slowed by an action on the ganglia of the sinus venosus (Steiner and Klapp). In warm-blooded animals the heart is also lessened in rapidity, but not by an action on the cardio-inhibitory apparatus seated in this organ; the blood-pressure rises greatly, partly by direct stimulation of the vaso-motor centre in the brain and the similar centres in the spinal cord.

The pupil is dilated, which Schiff states is due to the cramps changing the blood-gases, which act on the pupil. Klapp states that it increases intestinal peristalsis.

Action on Man.

In small doses it is thought to increase the appetite and aid digestion. In larger doses it produces great sensibility to external impressions, restlessness, stiffness, formication, the special senses are exalted in function, tremblings, then trismus, opisthotonos, and tetanus ensue, during which respiratory and cardiac action are imperceptible, the face is blue, and the eyes bulge out of their sockets. These convulsions are excited by touch, and are repeated till the person dies of asphyxia. It is excreted as such by the kidneys.

Action in Disease.

It is used in atonic dyspepsias, in paralysis of the nerves of the special senses and in paralysis of motor or sensory nerves of the spinal tract, and in reflex paralysis In the atonic dyspepsia its action may be explained by stimulating the nerves going to the stomach. In paralysis of the nerves of the special senses it excites their central origin, and in the spinal and reflex paralysis excites the spinal ganglia to activity.

BROMIDE OF POTASSIUM.

Damourette et Pelvet, Centralblatt, 1867; Laborde, Archives de Physiologie, vol. i, 588, 1868; Eulenberg u. Guttman. Virchow's Archiv, xli, p. 91; Lewisky, Virchow's Archiv, bd. xlv, p. 183; Schouten, Archiv der Heilkunde, xii, 2, p 97, 1871; Weil, Reichert's Archiv, 1861, p. 271; Bile, Am. Med. Journal, July, 1868; H P. Bowditch, Boston Med. and Surg. Jour., Oct. 1868; Amory and Clarke, Bromide of Potassium; Bartholow, The Bromides; Quincke, Reichert's Archiv, 1868, xxv, 158; Steinauer, Virchow's Archiv, bd. lix, p. 65; Krosz, Archiv f. Ex. Pat., bd. 6, 1 and 2 heft; Nunneley, Practitioner, 1869, p 347; Glover, Edinburgh Medical Journal, 1842; Voisin, Archives Generale, Janvier et Fevrier, 1873.

On Lower Animals.

Subcutaneously in frogs it causes fibrillary contraction of the muscles at the point of injection, where the muscles may even become tetanic. At length there is a loss of movement in the posterior extremities which extends to the anterior extremities. Finally there is complete abolition of all sensibility, whilst the voluntary movements persist. It abolishes reflex action by paralysis of the spinal sensory ganglia and Setschenow's centres. It reduces the frequency of the heart, causing arrest in diastole. In rabbits it increases the pulse and lowers blood-pressure. The effect of loss of sensibility may be the reason that the vagus allows the heart to run faster, as the nerves of sensation always keep it in a tonic state of activity. This would be an interesting question to work out The capillaries are stated by some to be contracted, by others to be dilated; the difference in results being probably the stage of poisoning studied and the dose. It slows the respiration and causes death by arrest of the respiratory centres. The tetanic effects observed in frogs seem to be due to increased muscular irritability. It reduces the temperature, and is excreted by the kidneys, saliva, and skin. It leaves the amount of urea lessened or unchanged, but increases the coloring, acidity, phosphates, chlorides, and uric acid; the carbonic acid given off by the lungs is decreased.

Krosz states that the metal potassium paralyzes the cardiac muscles, causes retardation of respiration, reduction of temperature, paralysis of the nerves and muscles; that the bromine produces pharyngeal anæsthesia, exanthema, and also slows the heart.

ON MAN.

It produces a drowsy feeling, tiredness of the muscles, anæsthesia of the pharynx, odor of bromine in the breath, diminishes the pulse and arterial tension, decreases the salivary secretion and temperature, makes the gait uncertain and memory poor. Krosz saw no contraction of the bloodvessels of the retina. When given in large doses bromism occurs, which is of two forms, the rapid and the slow. In the former there is considerable difficulty in the gait, falling of the eyelids, sleepiness, headache, diarrhœa, handwriting is tremblingly made and words are omitted; the tongue is red, dry, and large; there is great thirst. In the slow forms of bromism delirium appears accompanied with hallucinations, ideas of persecution, violence, ataxia of the extremities, and difficulty in speaking, or there is great stupidity, vision and hearing are enfeebled, memory is blunted, and the patient has all the symptoms of a drunken man except the anæsthesia of the skin. It depresses the sexual functions.

ACTION IN DISEASE.

This drug is mainly used in the treatment of epilepsy, chorea, hysteria, tetanus, and spermatorrhœa.

In epilepsy it acts in high doses by suppressing the play of sensory impressions on the cerebro-spinal axis, and probably by vaso-motor contraction of the bloodvessels of the medulla. This action also explains its effect in chorea, hysteria, and tetanus.

To explain its action as an antaphrodisiac the diminution of the reflex excitability of the spinal ganglia (Goltz's ganglia) with vaso-motor contraction are sufficient.

LOBELIA.

Ott, Physiolog. Action of Lobelina.

Lobelia inflata contains an alkaloid called lobelina.

On Lower Animals.

It produces loss of voluntary movement and co-ordination, paralysis of motor nerves, lessened reflex power of the spinal cord; it has no action on either the sensory nerves or the striated muscles. The pulse is at first slowed, then increased beyond normal, which is due to an action on the cardio-motor ganglia, supposing that atropia paralyzes the inhibitory ganglia. The arterial tension is temporarily depressed and then increased, the increase being due either to excitation of the peripheral vaso-motor system or the spinal vaso-motor centres.

Large doses paralyze the vaso-motor in the brain and the pneumogastrics. It accelerates the respiratory movements by an excitation of the pulmonary ends of the pneumogastrics; subsequently it reduces the respiration. It lowers the temperature.

On Man in Health.

It causes burning in the throat, nausea, emesis, muscular weakness, pulse weak, skin cold and perspiring, purgation may occur, trembling, agony, insensibility, and convulsions, ending in death. Lobelina has the same action as the root.

Action in Disease.

It is principally used in asthma, dyspepsia of a nervous origin, bronchial spasm, and as an emetic in pertussis and tetanus. How it relieves in asthma is not decided. Its irritation of the pulmonic terminations of the pneumogastric may reflexly prevent the spasm of the bronchial tubes.

NITRITE OF AMYL.

Richardson, Medical Times, 1863, No. 691; Brunton, Ludwig's Arbeiten, 1869, 101; Wood, H. C., Am. Med. Jour., cxxii, 39; Bernheim, Pflüger's Archiv, vii, 254; Hoffman, Reichert's Archiv, 1872, 746; Pick, Centralblatt, 1873, 865; Preyer, Die Blutkrystalle; Frederick u. Mayer, Archiv, f. ex. Path., bd. 5, 1, 11 heft; Amez-Droz, Archives de Physiologie, 1873, 467; Aldridge, West Riding Lunatic Asylum Report, vol. 1, p. 187; S. W. Mitchell, Philadelphia Med. Times, 1872, p. 262; Ladendorf, Centralblatt, 1875, p. 47; O. Berger, Centralblatt, 1875, p. 668; Bader, Centralblatt, 1875, p. 719; Burral, New York Medical Journal, 1875; Dabney, Virginia Medical Transactions, 187; Filehne, Pflüger's Archiv, bd. ix, p. 478; Brunton, English Journal of Physiology, vol. v; Schüllers, Dragendorff's Jahresbericht, 1874, p. 457; Bernhein, Pflüger's Archiv, 1873; Eulenberg, u. Guttmann, Reichert's Archiv, 1873; Lane, Journal of Diseases of Nervous System, July, 1877; Van Ermingen, Journal of Diseases of Nervous System, July, 1877.

On Lower Animals.

It diminishes the irritability of the motor nerves and muscles, and does not affect the sensory nerves till death. Consciousness remains till near the last. Locally it destroys muscular contractility. It diminishes reflex excitability by an action on the spinal cord. Convulsions are also seen.

The arterial tension is diminished with or without quickening of the heart's action. The action of the drug on the muscular walls of the arterioles is the cause of reduction of blood-pressure. The acceleration of the pulse in the rabbit is due to diminished irritability of the cardio-inhibitory centres.

The cardiac muscle is also greatly weakened in contractile force.

Death takes place through asphyxia. It increases the amount of urine, produces diabetes, reduces temperature, and diminishes excretion of carbonic acid. By an action on the blood, the two bands of oxyhæmaglobin become very faint, and an additional band appears in the same place as that of acid hæmatin. It forms a compound with the coloring matter of the blood and prevents the giving off and absorption of oxygen. It reduces but does not absolutely pre-

vent the oxidation of the blood through the respiratory apparatus.

On Man.

It lowers the temperature with at times a preliminary rise, dilates the bloodvessels, as in reddening of the face; the pulse runs faster and the arterial tension falls, with widening of the pupil, peculiar feeling in the head, and dizziness, which may be a result of the low pressure.

Action in Disease.

It is used in angina pectoris, asthma, migraine, and epilepsy.

In angina pectoris it acts probably by dilating the bloodvessels, and allowing the heart to relieve itself of its spasm. The same reason would apply in migraine with contraction of the arterioles. In asthma without organic lesion of lungs or heart, it may act by relieving the muscular spasm.

When there is time between the feeling of the aura and the onset of an epileptic fit, it can arrest the fit by a dilation of the bloodvessels, supposing that the convulsions of epilepsy are due to vaso-motor spasm of the medulla's bloodvessels.

Dr. Dabney has proposed it as an antidote in chloroform poisoning.

GELSEMIUM.

Barthlow, Practitioner, October; Ott, Physiolog. Action of Gelsemina; Ott, Physiolog. Action of Gelsemina and Gelseminic Acid; Berger, Centralblatt, 1875; Ringer and Murral, London Lancet, 1876 and 1877; Tweedy, London Lancet, June, 1877; Burdon-Sanderson, London Lancet, 1876; R. N. Taylor, Richmond and Louisville Med. Jour., 1876, No. 6; Wormley, Am. Jour. of Pharmacy; Sonnenschein u. Robbins, Berichte des Deutsch. Ges., Sept. 1876; Gray, New York Medical Record, 1876, No. 292.

Gelsemium contains two alkaloids, gelsemina and gelseminic acid, which, according to Professor Wormley, are united as gelseminate of gelsemina.

On Lower Animals.

Gelsemina destroys voluntary movement, increases and decreases spinal reflex excitability, produces convulsions, has no action on the motor nerves, muscles, and sensory nerves, reduces the heart-beat by an action on the excito-motor ganglia, and disperses the arterial tension by diminished tonus of the vaso-motor centre in the brain, decreases respiratory frequency by an action on the centres of respiration; the temperature of the body is also reduced.

Gelseminic acid convulses more than gelsemina, and causes a brilliant fluorescence of the humors of the eye; in other respects it acts on the nervous system like gelsemina. Artificial respiration will save poisoned animals.

On Man.

Gelsemina produces double vision, ptosis, want of co-ordination, disagreeable feeling in the head, great muscular relaxation, drooping of lower jaw, tongue stiff, sensation blunted, pupils dilated, respiration slow, irregular, pulse slow, surface cold and congested, unconsciousness, and death by asphyxia. Ringer and Murral state that during the diplopia the images in the upper part of the field of vision appear at different heights, although actually in the same plane. Locally the drug contracts the pupil, whilst internally it contracts and dilates it, paralyzing the third pair. The medicine affects the sixth nerve before the third, as the external rectus is the first muscle weakened. Taylor states that it increases the urine and reduces the pulse, respiration, and temperature. Tweedy states that it impairs the power of accommodation of the eye for near objects.

Action in Disease.

It is used in the Southern States in fevers of a sthenic type, where the diminution of pulse, arterial tension, and temperature afford an explanation of its value. It has

lately been lauded as an anti-neuralgic remedy, especially in trigeminal affections. It acts here by diminishing the excitability of the receiving ganglia. Piano-players' cramp and vesical irritability have been cured by it; here the same reason as in neuralgia comes into play.

HYOSCYAMUS AND STRAMONIUM.

Lawson, West Riding Lunatic Asylum Report, vol. v; Oulmont and Laurent, English Journal of Physiology, November, 1870; Laurent, Thèse pour le Doctorat, 1870; Harley, Old Vegetable Neurotics; Hellman, Beiträge d. Physiol. wirk. des Hyoscyamius; Pflüger, Centralblatt, No. 43.

Their alkaloids, hyoscyamia and daturia, resemble atropia in their action.

Action on Lower Animals.

They both act on the sympathetic, in small doses diminishing the capillaries, in large doses dilating them, consequently the arterial tension rises by small doses and falls after large ones, which is not prevented by section of the vagi. The heart and respiration are increased, they blunt peripheral sensibility, have no action on striated muscle, increasing in small doses peristalsis and in large doses arresting it. The general phenomena are due to circulatory changes; they dilate the pupil by exciting the sympathetic. Small doses increase, large doses diminish, the temperature. Both alkaloids are excreted by the urine.

Action on Man.

The symptoms of an overdose of stramonium and hyoscyamus are like those of belladonna. They dilate the pupil, cause nausea, retching, dryness of the throat, vertigo, delirium, and mental excitement. In larger doses the pulse is in the beginning depressed, afterwards increased. On the pupil hyoscyamia acts greater than datura or atropia. Whilst atropia and datura in large doses produce an eruption, hyoscyamia rarely does so. Furious delirium with great muscular weakness is generated by datura and atropia,

whilst hyoscyamia produces melancholy delirium alternating with stupor.

Atropia and datura paralyze in large doses the rectal and vesical sphincters, which hyoscyamia does not. In hyoscyamus poisoning there are convulsions as well as trembling of the limbs.

All these drugs have a hypnotic action similar to that of opium without the constipating effect.

Action in Disease.

Stramonium is usually employed in cigarette shape to relieve the attacks of asthma.

Hyoscyamus is used mainly as a hypnotic. Both drugs are used as an antineuralgic medicament and in the cases where belladonna is serviceable.

CHLORAL HYDRATE.

Richardson, Medical Times and Gazette, September 4th, 1870; Labbee, Archives Générale, 1870, tome xvi, p. 338; Andrews and Da Costa, Am. Med. Jour., April, 1870; Djurberg, Schmidt's Jahrbüch., bd. cli, p. 84; Tomaszewics, Pflüger's Archiv, ii, 35; Rajewsky, Centralblatt, 1870, p. 211; Liebreich, Tageblatt d 44, versam.; Deutscher Naturforscher u. Aerzte in Rostock, 1871; Levinstein, Centralblatt, 1875, p. 272; Meihuizen, Pflüger's Archiv; Brunton, Centralblatt, 1875, 304; Oré, Centralblatt, 1875, 485; Bouchut, Centralblatt, 1875, 636; Lewisson, Reichert's Archiv, 1870, 346; Byasson et Follet, Jour. d l'Anat et de la Physiologie, 1870, 579; Simonides, Pfluger's Archiv, v, 565; Liebreich, Practitioner, 1876; Amory, New York Medical Journal, 1870; Keen, Am. Med. Jour. 1875.

Action on Lower Animals.

In frogs there is an increase followed by a diminution of reflex action and of respiratory movement, with want of co-ordination. When they recover, breathing first becomes better, then reflex excitability and power of co-ordination. In warm-blooded animals the tactile sensibility is not as much affected as the thermic. On the brain it is excitant at first, afterwards depressant and soporific. It increases

and then diminishes respiratory action, the movement being irregular. It does not affect the motor nerves, and produces at times convulsions. It reduces the frequency of the heart, but not by cardio-inhibitory excitation. It reduces the arterial tension, paralyzing the chief vaso-motor centre. When a sensory nerve is irritated, Cyon states that the blood-pressure falls, but Heidenhain contradicts it. The respiratory apparatus always stops before the cardiac. The pupil is contracted, the temperature falls, and the urine is increased; the muscles are not affected. Chloral acts directly on the nerve-centres and not through an action on the blood. It is excreted, according to Von Mering and Musculus, as urochloralic acid. When the drug is mixed with an alkali in a test-tube, chloroform and formic acid are generated. Liebreich supposed that the bicarbonate of soda in the blood acting on the chloral produced formiate of soda and chloroform, the latter producing the peculiar hypnotic action. Chloral and chloroform given in conjunction prolong each other's action.

Action on Man.

It produces sleep and diminishes respiration, pulse, and temperature; reflex excitability is maintained. Death may take place either by respiratory or cardiac arrest. Dr. Keen has found it to be an excellent antiseptic.

Action in Disease.

It is used to produce sleep, in mania, delirium tremens, by its hypnotic action; to relieve convulsions, tetanus, and chorea and cramps by depression of reflex excitability; in parturition to relieve pain and relax the muscles. Liebreich states that it is an antidote to strychnia.

BUTYL-CHLORAL (CROTON-CHLORAL).

Liebreich, Centralblatt, 1877, 381; Wundelschmidt, Centralblatt, 1877, 912; J. V. Mering, Archiv f. Ex. Path., iii, 185-204; J. V. Mering, Centralblatt, 798, 1875; Ott, Atlanta Medical Journal, October, 1874.

ACTION ON LOWER ANIMALS.

In frogs, the cornea loses sensibility; loss of motion in anterior extremities, then loss of sensibility, of respiratory movement, of power to move the extremities; motor nerves preserve their excitability; heart's movements are arrested in diastole; thrusting probe down the spine excites very feeble movements. In rabbits the respiration and pulse are increased by minimum doses. Small doses lessen the respiratory frequency, leaving the pulse unchanged. Reflex action of cornea is lost, while general sensibility is retained. In large doses there is loss of reflex action and complete narcosis. When sensibility is restored, that of head appears last. It depresses arterial tension by paralyzing vaso-motor tunics. The pulse primarily is accelerated.

When death occurs the breathing is arrested before the heart, artificial respiration restoring the animal. If after poisoning with butyl-chloral the central end of the vagus is irritated there is no movement of the diaphragm, although irritation of phrenic moves it.

ACTION ON MAN.

In a child 2.5 grammes caused sleep from which the child was easily aroused by pinching. The cornea was anæsthetic, even when sleep had passed off; the nasal mucous membrane was sensitive. In an experiment on myself I took, by mouth, 0.32 gramme of this drug, and in thirteen minutes seemed to lapse into forgetfulness, and in eighteen minutes took 0.32 gramme more, when in twenty-three minutes the sensibility of face was less, it felt stiff; corneal sensibility less. In twenty-eight minutes took 1.6 gramme, and in about two

hours from the beginning of the experiment I could pass my finger over the cornea without pain; general sensibility and motility are good; the respiratory and cardiac apparatus does not seem disturbed; can walk about with difficulty; considerable sleepiness present; and in about five hours from the first dose the sensibility of the face and cornea was nearly normal.

Action in Disease.

It is used in trigeminal neuralgia for its anæsthetic quality in this region. It has occurred to me that in the extraction of foreign bodies from the cornea it would greatly relieve the pain often happening during extraction. It is superior to chloral in neuralgia, as it does not affect the heart in any great degree.

CONIUM.

Kölliker, Virchow's Archiv, x, 235; Damouette et Pelvet, Etude de Physiolog., Ex. et Therapeut. sur la cigue et sur Alcaloid; Lautenbach, Philadelphia Medical Times. vol. x, 186; Böhm, Die Herzgifte; Reuling u. Salzer, Deutsche Klinik, 1853, No 6; Albers, Deutsche Klinik, 1853, No. 34; Harley, Old Vegetable Neurotics.

Action on Lower Animals.

Locally it destroys the functions of nerve-centres, nerve and muscular tissue, and the blood-corpuscles.

It like woorari paralyzes the motor nerves; it increases and decreases spinal reflex excitability; produces convulsions, cerebral in origin, which are not diminished by artificial respiration; in large doses reduces the sensibility, and has no action on the muscles. It increases the heart-beat, and then slows it, whilst the arterial tension falls, and then rises above normal, the pneumogastrics being paralyzed. It increases the respirations by an excitant action on the endings of the vagi in the lungs, and afterwards decreases their irritability.

It causes in dogs vomiting and increased salivation; the

pupil is contracted, and then dilated through paralysis of the oculo-motor; the temperature is at first elevated and then depressed. The drug is eliminated by the lungs and kidneys.

On Man.

It causes increased salivary secretion, vertigo, diplopia, stiffness of tongue, inability to speak, feeling of paralysis in the extremities, with numbness; sweating; pupil dilates; difficulty in breathing. The pulse is very slow, convulsions sometimes occur, and sensibility is not affected till near death. It kills by paralysis of the respiratory apparatus; it is also antaphrodisiac.

Action in Disease.

It acts as an antineuralgic by its depressing reflex excitability. It is also used in diseases attended with muscular spasm, as in chorea, paralysis agitans, muscular twitchings, acting here by its paralytic action on the motor nerves. Its alterative action is not easily explained by any present physiological facts.

ERGOT.

Wernich, Centralblatt, 1873, 915; Holmes, Virchow's Archiv, iii, 384, Archives de Physiologie, tome iii, 1870; Rossbach, Pharmakolog. Untersuch., ii heft; Wenzell, Am. Jour. of Pharmacy, May, 1862; Haudelin, Schmidt's Jahrbüch, bd. clv, p. 143; Boldt, Schmidt's Jahrbüch., March, 1872; Brown-Séquard, Archives de Physiologie, 1870, vol. iii, p. 434; Bernheim, Centralblatt, p. 429, 1875; Wood, Philadelphia Med. Times, vol. iv.

It contains two alkaloids, ecbolina and ergotina, with an acid called sclerotic.

Action on Lower Animals.

In frogs, it slows the heart, and in large doses causes diastolic arrest by an action on the peripheral end of the vagus. It contracts the capillaries by an action on the chief vaso-

motor centre. A preliminary fall of pressure has been observed in rabbits before the rise of arterial tension, which has been thought by Holmes to be due to contraction of the pulmonary capillaries, causing less blood to be received from the right heart into the left. Rossbach observed that ecbolin produced a peculiar arythmia of the frog's heart. It excites the irritability of the trunks of the motor nerves, depresses that of the sensory nerves, and leaves the muscle intact. The temperature falls; the respiration is slowed. How it causes the uterus to contract is still doubtful. The experiments of Goltz and Freusberg show that the lumbar portion of the spinal cord is able to carry on the act of parturition, and make it quite probable that ergot acts on these centres in the spinal cord. It increases intestinal peristalsis.

Action on Man.

The chronic form of poisoning by ergotin is called ergotism, of which there are two varieties, the convulsive and the gangrenous. In the convulsive form, salivation, pain in stomach, vomiting, vertigo, continuous hunger, sleeplessness, tingling and burning of the skin, weakness, especially in the fingers and toes, followed by painful cramps of the hands and feet, which sometimes become tetanic, and death ensues. In the gangrenous form the pulse is small, scarcely perceptible, burning, tearing pain in the toes and lower extremities; the feet become gangrenous, which state travels upwards.

Sclerotic acid is a very active part of this drug.

Action in Disease.

Its vaso-motor constrictive power explains its use in hæmorrhages, congestions, and inflammatory disease of the spinal cord.

It is used to excite the uterine muscles to contract in the expulsions of fibroids, as well as to contract the arterioles and diminish the supply of blood to the tumors.

It has been lately used in enlarged prostate, where it may contract the prostatic capillaries.

TOBACCO.

Traube, Gesammelte Beiträge, 1, 302; Bernard; Nasse, Beiträge zur Physiologie der Dannbewegungen; Blatin, Virchow-Hirsch's Jahresbericht, 1870, 362; Heubel, Pflüger's Archiv, 1874; Uspensky, Reichert's Archiv, 1868, 522; Von Basch und Oser, Untersuch. üb. die Wirk des Nicotin; Benham, Centralblatt, 1875, p. 320; Tscheschicin, Reichert's Archiv, 1866, 151; Haynes, Phila. Med. Times, May 12th, 1877.

This drug contains an alkaloid, nicotin, upon which its active properties depend.

On Lower Animals.

On the frog, it produces spinal clonic convulsions; the anterior extremities are placed against the body, whilst the posterior extremities are drawn up over the back, so that the feet touch each other; the motor nerves are paralyzed, and the reflex excitability is diminished; the muscles are not affected; the endings of the motor nerves in the muscles are irritated, as there are fibrillary twitchings.

In warm-blooded animals, convulsions, not excited by touch, ensue, and are not prevented by artificial respiration. The convulsions persist after decapitation.

The pulse and arterial tension in the short first stage fall, then rise, then they sink, and finally the pressure is very low, and the pulse increases. The variations in the pulse are the result of an excitation of the vagi with their subsequent paralysis. The blood-pressure is elevated by excitation of the vaso-motor system, and depressed by vaso-motor paralysis.

The respirations are at first accelerated, and then slowed. Nasse saw the uterus and intestines thrown into active movements by nicotin, a statement which I can confirm. The cause of this is probably in an excitation of the ganglia seated in the walls of the intestine. Nicotin destroys the

inhibitory power of the splanchnics over the intestinal movements.

Action on Man.

This produces a disagreeable burning taste in the mouth and increased salivation, followed by nausea, vomiting, and diarrhœa, excitation, dizziness, headache, rapid pulse, great muscular prostration, sometimes clonic convulsions, difficult respiration, partial unconsciousness, cold extremities, general collapse, and death.

Action in Disease.

This drug is used to produce relaxation in hernia, in asthma, in tetanus, and poisoning from strychnia. Here its paralyzing power over the motor nerves comes into play.

JABORANDI.

Riegel, Centralblatt, 1876, No. 15; Stumpf, Pilicier, Craig, Centralblatt, 1876, No. 24; Köhler und Soyka, Centralblatt, 1876, No 31; Hardy et Rochefontaine, Centralblatt, 1876, No. 32; Schwan, Centralblatt, 1876, No. 25; Ringer and Gould, London Lancet, 1874, i, No. 5; Ohne, Lorisch, u. Robin, Centralblatt, 1875, p. 623; Tweedy, London Lancet, Jan. 1875; Langley, English Journal of Physiology, 1876 and 1877; Frommüller, Centralblatt, 1877, No 7; Tyson and Bruer, Am. Med. Jour., July, 1877.

This drug contains an alkaloid, pilocarpin, and organic matter.

Action on Lower Animals.

It excites the salivary secretion by peripheral irritation of the chorda tympani, which is removed by atropia. It increases the gastric secretion, intestinal peristalsis, and, according to Vulpian, the biliary secretion, which Pelicier contradicts. In the frog it slows the heart, which slowing is due, according to Langley, not to pilocarpin, but to other organic matter. Langley states that pilocarpin paralyzes the vagus. It at first accelerates and then slows the pulse.

The other organic material excites the cardio-inhibitory ganglia, which excitation is removed by atropia. The arterial tension is reduced, which fact one of my pupils, Mr. Physick, has confirmed on rabbits.

Pelicier saw in cats and dogs trembling, and in large doses dyspnœa and light spinal convulsions. In them the gastric secretion is increased. According to Pelicier its action is similar to that of muscarin.

Action on Man.

It strongly excites the cutaneous and salivary secretion, and, according to some, the bronchial and lachrymal, the secretion of sweat following that of saliva in five minutes. The sweat is at first acid, later neutral, and sometimes slightly alkaline. The organic elements and ferrocyanide of potassium in the saliva are increased, so that on the whole the quantity of solids is merely slightly lessened. It causes nausea, vomiting, and diminished quantity of urine, pain in head, with disturbances of vision; the pulse is at first fuller and more frequent, but afterwards is very often small; the face is pale, the respirations accelerated, then slowed; the temperature is reduced, and pupil contracted. The drug increases the tension of the power of accommodation, and impairs vision by making the retina less sensitive. The sweating may amount to as high as fifteen ounces, the chlorides being in excess, and the urea by the skin greatly in excess of normal. The urea by the kidneys is increased.

Action in Disease.

It has been used in diabetes, and as a diaphoretic in fevers, and in Bright's disease.

SALICYLIC ACID.

Butt, Centralblatt, 1875; Drasche, Centralblatt, 1875, No. 10; Farsky, Centralblatt, 1877, No. 13; Binz, Centralblatt, 1877, No. 43; Johannsen, Centralblatt, 1877, No. 5; Hiller, Centralblatt, 1877, No. 5; Fischer, Centralblatt, 1877, No. 5; Köhler, Centralblatt, 1877, No. 10; Pel, Centralblatt, 1876, No. 27; Bäer, Centralblatt, 1877, No. 23; Petersen, Centralblatt, 1877, No. 18; Furbringer, Centralblatt, 1875; Miller, Phila. Med. Times, 1875.

On Lower Animals.

It reduces the blood-pressure by an action on the heart's ganglia and muscles. The pulse is also slowed. The vagus shortly before death is inexcitable. By the mouth the cardiac functions were not affected, the respiration being slowed. Salicylic acid in the shape of salicylate of soda acted like the acid on the heart even when taken by the stomach, only the irritation of the sensory nerves here elevates the arterial tension for a short time. Both the acid and salicylate of soda retard the respiration and lower the temperature, the soda compound decreasing it more than the acid. It occasions mortal asphyxia, convulsions, and does not increase the urinary secretion.

Action on Man.

It occasions great pain in the head, roaring in the ears, weak vision, profuse sweat, hallucination, mydriasis, divergent strabismus, and difficulty in speech. It is excreted by the kidneys.

Action in Disease.

It is used in typhus and intermittents to reduce the temperature. It is used in rheumatism and to prevent fermentation. It is employed largely in the place of carbolic acid to dress wounds, here destroying the low organisms.

CALABAR BEAN.

Christison, Edinburgh Med. Jour., xx, 1855, p. 193; Fraser and Robertson, Edinburgh Med. Jour., 1863, 1st part, 36, 123, 235, and 1863, 2d part, 815; Watson, Edinburgh Med. Jour., 1866, p. 999; Bauer, Centralblatt, 1866, p. 577; Laschkewich, Virchow's Archiv, xxv, 291; Bezold u. Götz, Centralblatt, 1867, p. 241; Gscheidlen, Untersuch. aus dem Physiolog Laboratorium in Würzburg, viertes heft; Tauchau Archiv d. Heilkunde, vi, 69; Arnstein u. Sustschinsky, Untersuch. aus dem Physiolog. Laboratorium in Würzburg, drittes heft; Heidenhain, Pflüger's Archiv, v, 40; Böhm, Die Herzgifte; Grunhagen, Virchow's Archiv, bd. xxx, p. 481; Papi, Schmidt's Jahrbüch, bd. cxlii, p. 287; Leven u. Laborde, Schmidt's Jahrbüch, bd. cxlvi. p. 136; Westermann, Schmidt's Jahrbüch, bd. cxxxviii, p. 29; Rossbach, Pharmako. Untersuch., i heft, 1873; Kohler, Archiv f. Ex. Path., heft i, 1877; Frazer, Transactions of Royal Society, xxiv, 3, 1877.

The alkaloids of this drug, upon which its virtues depend, are eserina, or physostigma, and calabarin, which acts like strychnia.

On Lower Animals.

In frogs, it excites the peripheral terminations of the motor nerves, causing fibrillary contraction of the muscles; then the motor nerves are paralyzed. It also paralyzes by an action on the central nervous system. The reflex activity of the spinal cord is greatly depressed. The muscles and sensory nerves preserve their irritability. It sometimes occasions in frogs tetanus, probably due to calabarin. In warm-blooded animals it kills by arrest of the respiration from paralysis of the centres of respiration. It at first causes an acceleration of the movements of breathing by an irritation of the peripheral end of the vagi, and finally slows the movement. Artificial respiration will restore animals. It slows the heart by an excitation of the cardio-inhibitory centres, which is removed by atropia and saponin, and restored by a subsequent dose of calabar. Large doses of this drug do not paralyze the vagi. The arterial tension is elevated by a cramp of the muscles in the walls of the intestine. It increases the secretion of saliva by a peripheral irritation of

the chorda tympani. It contracts the pupil by irritation of the oculo-motor ends in the pupil, and produces a cramp of accommodation; the temperature is also reduced.

Action on Man.

It occasions nausea, emesis, disturbances of vision, vertigo, muscular weakness, reduction of heart-beat, sweating, and narrowing of the pupil, dyspnœa, and increase of salivary secretion. It causes myosis and cramp of the accommodation. Fraser has shown that on the administration of atropia the effect is antidotal.

Action in Disease.

It is used in tetanus because it paralyzes the motor nerves and reduces reflex excitability, and in dilatation of the pupil, where there are synechiæ, to break them up, and in paralysis of the power of accommodation, and the oculo-motor nerve, to restore them.

Care must be taken that it contains no calabarin, which tetanizes.

BELLADONNA.

Harley, Old Vegetable Neurotics; Da Costa, Am. Med. Journal; Mary Putnam, New York Med. Record, 1873; Botkin, Virchow's Archiv, bd. xxiv, p. 83; Jones, Medical Times and Gazette, 1857; Hayden, Dublin Quarterly, 1863, p. 51; H. C. Wood, Jr., Am. Med. Jour., April, 1873; Böhm, Archiv f. Ex. Path., iv, 8; Keuchel, Das Atropin; Englehardt, Untersuch. aus d. Physiolog. Laborator. in Würzburg, viertes heft; Donders, The Accommodation and Refraction of the Eye; Bernard, Physiologie du Système Nerveux, vol. ii, p. 212; Wood, Phila. Med. Times, vol. i, p. 29; Rossbach u. Fröhlich, Pharmakolog. Untersuch., 1873; Schmiedeberg, Ludwig's Arbeiten, v, 1870; Böhm, Die Herzgifte; Heidenhain, Pflüger's Archiv, v, 40; Ringer and Murral, English Journal of Physiology, 1876; Fraser, Transactions of the Royal Society, vol. xxv, 1869; Norris, W. F., Am. Med. Journal, 1862; Von Bezold u. Blöbaum, Würzburger Untersuch., i, 1867; Reese, Am. Med. Journal, vol. xi.

Action on Lower Animals.

It paralyzes the motor nerves in frogs at the same time that it excites the spinal cord; after they recover from the

motor nerve paralysis the tetanic symptoms of spinal stimulation appear. The sensory nerves are affected. The muscles are not paralyzed. In warm-blooded animals it increases the pulse by paralysis of the inhibitory ganglia seated in the heart. Very small doses slow the heart by excitation of the cardio-inhibitory ganglia. Large doses of atropia paralyze the cardio-motor ganglia; the blood-pressure is elevated by the contraction of the arterioles. Large doses reduce the arterial tension by a dilatation of the arterioles and weakness of the cardio-motor apparatus. It at first slows and then increases respiratory movement, the slowing being due to a paralysis of the vagus-ends in the lung. It removes the influence of the chorda tympani over the salivary gland, and of the splanchnics over the intestinal movements. It dilates the pupil by paralyzing the oculo-motor endings. Kieser and Wood first pointed out that it did not dilate the pupil in birds. Rossbach states that very small doses first contract the pupil.

It is excreted by the kidneys, and produces a state of muscular relaxation of the intestines, bladder, and uterus.

Action on Man.

Here the pupil is dilated, does not contract when exposed to the light; the head aches; the mouth and throat are dry; the skin is not bathed with perspiration as usual; there is redness of the face; restlessness, drunken-like delirium alternating with hallucinations and somnolency; speech is difficult, and the erect position lost.

Action in Disease.

In diseases of the eye it is used to dilate the pupil to prevent synechiæ, and to diminish the supply of blood.

Its power to relax the involuntary muscles will explain its utility in rigid os uteri, and spasms of the sphincters, and constipation.

Its power to benumb sensory nerves explains its value in pertussis in children, asthma, and incontinence of urine.

Its power to make the skin hot and dry explains its value in the arrest of nightsweats.

In neuralgia it seems to be of service, probably by a sedative action on the central ganglia.

In opium-poisoning it is the great antidote when given subcutaneously. It acts here by exciting the respiratory centres to action, and in allowing the heart to send more blood to them.

It will also be of great value after poisoning by mushrooms, removing the depression of the heart caused by the irritated cardio-inhibitory centres.

In all cases where death is by central respiratory paralysis it will probably prove useful, by its great power of stimulating the centres of respiration.

MUSCARIN.

Alison, London Medical Record, June 15th, 1876; Schmiedeberg u. Koppe, Das Muscarin, Leipzig, 1874; Prevost, Centralblatt, 16, 1875; Ott, Journal of Nervous Diseases, 1876; Schiff, London Medical Record, August, 1876; Schmiedeberg u. Harnack, Centralblatt, 1875, No. 36; Hamilton and Sweezy, New York Medical Record, November, 1876.

This alkaloid is found in Agaricus muscarius, a poisonous mushroom, and probably is the main toxic agent in all poisonous mushrooms.

On Lower Animals.

On cats subcutaneously it causes chewing or licking movements, profuse flow of saliva, increased lachrymal secretion, colic, vomiting, increased intestinal peristalsis, purging, which is often bloody, tenesmus-like pain, increased flow of saliva, which depends on peripheral stimulation of the chorda tympani, and narrowing of the pupil. All these phenomena can take place before the movements are interfered with. The cause of death is seated in the respiratory apparatus. The heart-beat is accelerated and reduced by an excitation

of the cardio-inhibitory apparatus seated in the heart. The arterial tension is lowered, probably by a dilatation of the bloodvessels. This alkaloid does not seem to have any direct action on the nervous system.

Muscarin excites the chorda tympani, atropia paralyzes it; muscarin excites the cardio-inhibitory apparatus, atropia paralyzes it; muscarin contracts the pupil, atropia dilates it; muscarin increases intestinal peristalsis, atropia decreases it; muscarin decreases the urinary secretion, atropia restores it.

It also produces a cramp of the accommodation of the eye, which reaches its maximum in fifteen to twenty minutes, and passes away in a few hours. In some respects it acts like calabar bean. Like it, it causes tetanus of the intestinal tract, it contracts the pupil, produces cramp of accommodation, and excites the cardio-inhibitory apparatus, which excitation is removed by atropia, restored by calabar, but not by muscarin.

Action on Man.

In three to five milligrammes it causes profuse salivation and rush of blood to the head, redness of the face; the brow is moist; vertigo ensues, with griping and colic, large drops of perspiration standing out on the face. The disturbed vision in connection with the vertigo and weariness of the head have a remote similarity to the action of alcohol.

Action in Disease.

Dr. Sweezy employed it in a case of posterior spinal sclerosis, where it abated the severe pain in the limbs.

ERYTHROXYLON COCA.

Bennet, Edinburgh Medical Journal, October, 1873; Moreno y Maiz, Recherches Chimique et Physiologique de l'Erythroxylon Coca; Ott, Coca, Veratria, and Gelseminum, 1874; Bucheim u. Eisenmenger, Eckhard's Beiträge, v bd. ; Mantegazza, Encyclopædia Igienica Populare.

This plant's leaves contain for their active principle an alkaloid called cocain.

On Lower Animals.

In frogs, small and large doses cause loss of co-ordination and decrease of power in the motor nerves.

In small doses it tetanizes upon the least irritation, whilst large doses abolish the functions of the posterior columns and sensory nerves. It prolongs muscular contraction and dilates the pupil.

Death takes place by arrest of the respiratory apparatus. Here the centres are paralyzed. In rabbits, the pulse and arterial tension fall, succeeded by a subsequent rise of both. In dogs the pulse and pressure after small doses rise, after large doses fall and then rise. This action of the drug is due to an action on the cardio-motor apparatus and the vaso-motor system. It does not paralyze either the pneumogastric or the vaso-motor centre. It increases and then reduces the temperature.

Action on Man.

After a small dinner with a cup of coffee I masticated some coca, swallowing saliva and leaves. At first there was increased salivation, warmth of buccal mucous membrane, which extended to the stomach; the taste of leaves was at first rather bitterish, afterwards sweet-like; the heat of the skin seemed increased, and the physical forces seemed greater. In thirty-five minutes there was a slight disposition to move about. In two hours and a half ten grammes were eaten and some intoxication was present; co-ordination impaired; muscular strength seemed weakened, a sort of paresis; disposition to go into reverie, with frontal pain; tinnitus aurium; ears feel as if I had been blowing a wind instrument; pupil slightly dilated. In three hours somnolency, frontal pain, and fulness about ears; disposition to close the eyelids; general numbness of the whole body. In three hours and twenty-five minutes, twenty-nine cubic centimetres of water taken; mouth hot and dry, nervous urine passed. In three hours and forty-five minutes, reveries, holding of respiration

as in deep thought. In four hours, nineteen and a half grammes of coca leaves were chewed and swallowed; the remaining coca taken was only chewed and the saliva swallowed; somnolency disappearing, mind bright and clear. In five, hours twenty-eight grammes taken; pupil more dilated; slight supper taken, no coffee. The supper seemed to lessen the action of the coca. In seven hours and forty minutes, coca being chewed, the frontal headache and fulness of ears return. In eight hours and forty-five minutes, sixty grammes of coca have been chewed; loquacity, eyes brilliant and moist, speech thick; in high spirits. In ten hours and fifteen minutes, frontal headache again coming on, drowsiness; retire, but am unable to sleep. After a few hours deep sleep supervenes.

In man it increases the pulse and temperature. It decreases the urea and increased my weight. The urine contains oxalate of lime crystals, which are contained in the leaves. It is excreted by the kidneys.

As is seen in the effects, coca and cocain resemble the action of coffee and caffein. Among the Peruvians it is used like tobacco, and supports their strength in arduous labor.

Action in Disease.

It is used in mercurial stomatitis, inflammation of the gums, painful dyspepsia, gastralgia, and phthisis. In mercurial stomatitis and gingivitis its benumbing effect on the mucous membrane comes into play as well as in gastralgia. In phthisis its power to retard retrograde metamorphosis is important.

CHLOROFORM, ETHER, AND NITROUS OXIDE.

Kussmaul, Virchow's Archiv, xiii, p. 289; Böttcher, Virchow's Archiv, xxxii, p. 126; Hermann, Pflüger's Archiv, 1866, p. 27; Bernstein, Schmidt's Jahrbüch., bd. cxlii, p. 227; Bucheim u. Eisenmenger, Eckhard's Beiträge, v, 73; Dumeril et Demarquay, Archives Générale, 1848; Westphal, Virchow's Archiv, xxvii, 409; Snow, On Anæsthetics; Husemann, Schmidt's

Jahrbüch., bd. cli, p. 84; Hering u. Kratschmer, Berichte der Wiener Akademie, lxii, bd. ii; Knoll, Sitzb. der Kaiserlich Akademie der Wissen. 1873; Vierordt, Archiv f. Physiolog. Heilkunde, 1856, 269; Gosselin, Archives Générale, 1848; Scheinesson, Archiv d. Heilkunde, x, 37, 172, 225; Anstie, Stimulants and Narcotics; Bowditch and Minot, The Influence of Anæsthetics on Vaso-motor Centres; Bernard, Leçons sur les Anæsthesiques et sur l'Asphyxiæ; Nothnagel, Handbuch der Arzneimittellehre, 1874; H. Köhler, Handbuch d. Physiolog. Therapeutik, 1876; Dogiel, Reichert's Archiv, 1866.

ETHER.

Bernard, Substances Toxiques, 413; Wittich, Schmidt's Jahrbüch., bd. cxii, p. 212; Herrman, Archiv f. Anat. u. Physiologie, 1866, 27.

NITROUS OXIDE.

Amory, New York Med. Jour., Aug. 1870; Jolyet et Blanche, Archives de Physiologie, July, 1873; Thompson, Phila. Medical Times, Nov. 1873; Herrman, Lehrbuch der Experimentellen Toxicologie, 1874.

CHLOROFORM.

Action on Lower Animals.

In all animals it narcotizes, rabbits and dogs being difficult to bring under its influence. The respiratory movement ceases before that of the heart. Injection into the veins arrests the heart, causing a rigor of the muscles. The ascending part of the muscle-curve is very much lengthened. The voluntary muscles are affected like those of the heart when it is injected into the abdominal aorta. The temperature is reduced, as well as the arterial tension. The pulse is accelerated and then slowed. When a rabbit inhales chloroform or any irritant gas, the local excitation of the gas on the endings of the trigeminus is reflected on the heart and respiratory apparatus, inhibiting their action. Chloroform accelerates and then retards respiratory action. The pupil is contracted by central excitation of the oculo-motor nerve, and dilated by its paralysis. Pinching the skin in chloroform anæsthesia will dilate the pupil, as happens normally. It dissolves out the hæmoglobin of the red corpuscles, forming a lake, and the union of oxygen with the hæmoglobin is

firmer than is normal. The muscles and nerves of chloroformed animals are irritable. The fall of blood-pressure is due to paralysis of the vaso-motor centre in part, and to weakening of the heart. The slowing of the heart is due to an excitation of the cardio-inhibitory apparatus. The action of chloroform can be prolonged by the subcutaneous use of morphia.

Both chloroform and ether first affect the cerebral hemispheres, then the cerebellum, spinal cord, peripheral nerves, and medulla oblongata, in the order named.

Action on Man.

In the first stage there is excitation of the senses, with increase of the pulse and arterial tension. It produces anæmia of the brain. The physical forces are increased, attended with singing, profanity, laughing, and so on. In the second stage there is a loss of the sense of pain and of general sensibility, followed by progressive loss of motility. In the third stage there is complete loss of consciousness, narcosis, and immobility. The pupil is narrowed, pulse decreased, respiratory movement is feeble, and muscular relaxation is complete. The recovery is similar to that of a person awaking from a profound slumber. The causes of death are divided into three classes: Syncope, apnœa, and gradual asphyxia. By the syncopal form the pulse stops suddenly, the heart is arrested, the face pale, and pupil dilated. In the apnœic form the breathing stops suddenly, the heart still beating. In the form of gradual asphyxia, the breathing is irregular and stops. In large doses by the mouth it causes gastro-intestinal inflammation. How anæsthetics act is still doubtful, as Lewisson has shown the nervous system may be affected without the presence of blood. It is quite probable that they affect the nervous system by a direct chemical action on it.

ETHER.

Here the symptoms are analogous to those of chloroform.

The stage of excitement is longer, and after the removal of the sponge the person soon recovers from the narcosis. The danger of arrest of the cardiac or respiratory apparatus is less by ether. Ether elevates the arterial tension, which remains a long time. The heart pulsates for a considerable time after death. Bowditch and Minot state that apparently the vaso-motor centre was excited and then depressed. The arterial tension is increased.

NITROUS OXIDE.

Action on Lower Animals.

Frogs, when immersed in the gas, become dyspnœic and die. Warm-blooded animals become restless, have dyspnœa, convulsions, and die from asphyxia, the blood being dark. Muscles, nerves, and the frog's heart die when placed in the gas. Amory states that the cerebral pulsations are diminished, but the arterial tension is increased. It has very little or no influence on the motor nerves.

Action on Man.

When inhaled it gives a sweet taste, roaring in the ears, a feeling of warmth over the whole body, a sense of fulness, pressure in the head, and insensibility.

Dr. Amory has shown that the arterial pulsations are lessened, that the cerebral arterial tension is increased, and that it diminishes the amount of carbonic acid exhaled. The pupil is dilated. This gas seems to produce unconsciousness mainly by asphyxiating the person.

Action in Disease.

Chloroform and ether are principally used to abolish consciousness, to relieve the pain of labor, spasm of the ducts, and convulsions.

Ether is very frequently preferred to chloroform for the

production of insensibility, as the former is not so paralyzing to the respiratory and cardiac centres.

Nitrous oxide acts as an anæsthetic mainly by asphyxiating.

When ether and chloroform produce dangerous symptoms, the lowering of the head, or inhalation of nitrite of amyl, retards the anæmia superinduced by them.

OPIUM.

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MORPHIA.

Action on Lower Animals.

With frogs it produces sleep, heightened excitability, spinal convulsions, and finally general paralysis. In dogs it produces masticating movements, howling, and sleep, with

snoring breathing. On awakening, a little slap produces considerable excitement. The gait is hyenoid. In rabbits it produces with difficulty sleep and frequently convulsions. In rabbits and dogs, for the most part, it slows and then accelerates the heart. If large doses are given, there is slowing of the pulse. If the vagi are previously divided, there is no retardation, but acceleration. The slowing is due to central and peripheral cardio-inhibitory excitation. Large doses paralyze the vagi. The primary acceleration of pulse may be due to excitation of the accelerators. The arterial pressure in the beginning is elevated, due to stimulation of the main vaso-motor centre. During the slowing of the pulse, the arterial tension is depressed, due to vaso-motor paralysis and cardiac debility, probably seated in the cardiac ganglia. Respiration is reduced by an action on the respiratory centres. In dogs it produces a great flow of saliva. It narrows the pupil, perhaps by stimulation of the oculo-motor endings. Intestinal peristalsis is increased; the excitability of the motor nerves in frogs is first increased and then depressed by large doses. It excites the sensory nerves. It produced veratroid contraction in the experiments that I made with striated muscle. It increases and then decreases reflex excitability. On pigeons, ducks, and chickens it has no influence.

Action on Man.

The action of opium is very similar to that of morphia. Morphia causes excitement, acceleration of the pulse, followed by its reduction, the breathing is hurried, and then slowed; the skin is at first red and tingling, then pale, with sweating, headache, nausea, vomiting, dryness of the mouth, and narrowing of the pupil, and sleep. By the vein it causes vertigo, roaring in the ears, bitter taste, prickling of the skin, palpitation of the heart, coma, and even death. In some cases it produces great prostration, nausea, vomiting, and in others delirium and convulsions.

ACTION IN DISEASE.

Opium or morphia is given to calm pain, procure sleep, arrest exhausting discharges, to produce relaxation of the muscular system in spasmodic states, and to allay irritations, as in cough. It checks diarrhœa by an anexosmotic effect. It produces sleep partly through a contraction of the capillaries of the brain, and partly by an action on the constitution of the molecules of the nerve-matter.

It is of great value in fevers and inflammations. In poisoning by opium, the use of atropia subcutaneously in one-hundredth of a grain doses or larger, is the best treatment as an antidote.

CODEIA.

ACTION ON LOWER ANIMALS.

In frogs it produces sleep, heightened excitability, and spinal convulsions. Wachs noted a peculiar gait in frogs, due to want of innervation in the adductors.

I have seen this also with other alkaloids of opium, one leg being extended, whilst the other is drawn up. In pigeons it produces violent convulsions. In dogs it produces sleep. Falck states that it produces two kinds of effects, tetanic and soporific. It paralyzes in frogs the posterior extremities and weakens the heart; respiration is diminished; produces cramp and convulsions of the stretching kind. In my experiments with codeia on frogs, it was narcotic and convulsivant. The action of the frog's heart was lowered by an action on the cardiac muscle. The striated muscles show a veratroid-contraction curve.

ON MAN.

On myself it was a hypnotic, followed by considerable gastric disturbance.

NARCEIN.

On Lower Animals.

In frogs it produces excitement, a half-comatose state, without any important alteration of the breathing or heart-beat. In frogs I saw narcosis and convulsions, the convulsions being partly spinal and partly muscular. The muscle-curve was veratroid. It reduces the action of a frog's heart, by an action on the cardio-inhibitory apparatus.

On Man.

In my own person, I have never seen the slightest hypnotic effect, and Drs. Mitchell and Da Costa have already made a similar statement. Other observers state that it is a hypnotic.

THEBAIN.

Action on Lower Animals.

It is a spinal tetanic agent, not acting on the motor, sensory nerves or muscles. In mammals, there are three stages of action by it; in the first stage, restlessness, tendency to hide, increased respiratory movement; in second stage, violent tetanus; in third stage paralysis, ending in death. In mammals I have shown that it increases arterial tension by stimulating the main vaso-motor centre.

On Man.

It appears to have no effect, although Eulenberg saw .004 gramme cause increase of the respiration, pulse, and temperature, with dilated pupil.

CRYPTOPIA.

Action on Lower Animals.

In moderate doses in frogs, it slows cardiac movement, large doses completely arresting the heart by paralysis of the

cardiac muscle. Large doses also paralyze the respiratory apparatus, causing death. It at first excites and then paralyzes the respiratory centres. The excess of carbonic acid produced by respiratory arrest excites convulsions. It reduces the excitability of the spinal cord, motor nerves, and muscles.

In warm-blooded animals the cardiac contractions were reduced independent of the lessening of respiratory frequency. In experiments on frogs there was frequency of breathing, dilatation of the pupil, loss of co-ordinating power over the extremities, a lower excitability of the motor nerves. It increased and then decreased reflex excitability by an action on the spinal cord. The height of the muscle-curve was less than normal.

Action on Man.

It is a pleasant hypnotic, one-fourth as powerful as morphia.

PAPAVERIN.

Action on Lower Animals.

Bernard thinks it is a convulsivant, whilst Baxt states that it is possessed of hypnotic qualities, reducing the heart-beat in frogs by stimulation of the cardio-inhibitory apparatus. With frogs I have seen it produce a semi-comatose state and convulsions, which are partly spinal and partly probably muscular. It produces on striated muscle a veratroid contraction.

On Man.

It was a hypnotic in my case.

NARCOTIN.

On Lower Animals.

Baxt, on frogs, states that it is convulsivant, and produces a semi-comatose state. With frogs, I have seen it produce

hyperæsthesia and spinal convulsions. It greatly slowed the frog's heart by an action on cardiac muscle.

On Man.

I experienced no effect from it.

MECONIN.

On Lower Animals.

Dr. Mitchell, on pigeons, saw an emetic effect, whilst Harley believes it has a weak hypnotic action on frogs. I have seen it produce hyperæsthesia and subsequent relaxation with a little sleepiness. It has little or no action in small doses.

On Man.

I have seen no soporific effect.

Apomorphia is an emetic, even in asphyxia, when introduced subcutaneously.

Cotarnin is soporific, and paralyzes the motor nerves like woorari.

Laudanin and laudanosin are tetanic agents.

Oxymorphia has an action like morphia, only weaker.

I give, in the following table, the action of many of the elements of opium, in the order of their strength, as near as I could ascertain:

NARCOTIC EFFECT.		CONVULSIVANT EFFECT.	TOXIC EFFECT.	
Man.	Animals.	Animals.	Man.	Animals.
Morphia. Codeia. Cryptopia. Papaverin.	Morphia. Codeia. Cyptopia. Narcein. Meconin.	Thebain. Laudanin. Laudanosin. Hydrocotarnin. Papaverin. Narcotin. Codeia. Morphia.	Morphia. Codeia. Cryptopin. Thebain. Papaverin. Narcein. Narcotin.	Thebain. Laudanin. Laudanosin. Hydrocotarnin. Morphia.

ELECTRICITY.

Remak, Galvanotherapie; M. Rosenthal, Die Elektrotherapie; E. Cyon, Principes d'Electrotherapie; Fick, Medicinische Physik; Morgan, Electro-Physiology; J. Rosenthal, Electricitätslehre; Rabuteau, Elements de Therapeutique; Grehant, Manuel de Physique Medicale; Pflüger, Untersuch. über die Physiol. des Electrotonus; Heidenhain, Physiologische Studien.

Electricity is of two kinds, static and dynamic. The static is generated by the friction of plate glass upon cushions, one kind going to the glass, and the other to the cushions. This kind of eleetricity is little used.

Dynamic electricity is generated by the chemical action of a fluid on a metal. In the zinc and copper element the electricity is developed by the zinc being used up by the acid, the copper being but little acted upon. The direction of the electrical current is always from the corroded metal, as the zinc is negative and the copper positive. The union of metals is called a "*cell*," their binding wire a "*conductor*," and the acting capacity of the cell its "*electro-motor force.*" In the explanation of the action of electricity I shall follow Cyon, who has given in his work the most thoroughly scientific exposition of this complicated subject.

Ohm discovered a law which is, that the intensity of the current is proportional to the electro-motor force. It can be formulated thus:

Let I represent the intensity of the current, E the electromotive force, and R the resistance of the conductor:

Then, $I = \frac{E}{R}$. This fundamental law is to be recognized in all studies in the application of electricity. The resistance usually met with is divisible into two parts: 1. The resistance of the circuit by the human body, electrodes, and conducting wires, called external resistance. 2. The resistance of the cell itself, by the liquids which must be traversed by the electric current, is named internal resistance. If the

external resistance should be represented by r, and the internal resistance by R, the law will be as follows, when formulated: $I = \frac{E}{R + r}$. If there is a number of elements, the equation will be $I = \frac{nE}{nR + r}$, n representing the number of cells.

The two extreme cases which are presented in the practical application of electricity will be now considered.

If the external resistance in comparison with the internal resistance is overlooked, then the formula

$$I = \frac{nE}{nR + r} \text{ will be } I = \frac{nE}{nR} = \frac{E}{R}.$$

Hence the law is deduced, *that when the resistance of the circuit in comparison with the resistance of the element is overlooked, the intensity of the current is not augmented by increasing the number of the elements.*

If the internal resistance in comparison with the external resistance is overlooked, then the equation $I = \frac{nE}{nR + r}$ will be $I = \frac{nE}{r}$, from which the second law is evolved, *that when the internal resistance in comparison with the external resistance is overlooked, the intensity of the current increases with the number of the elements.*

If the surface of the element is increased n times, the resistance becomes n times smaller (taking a transverse section), and the formula will be $I = \frac{E}{\frac{R}{n} + r}$, and if r is neglected, then $I = \frac{E}{\frac{R}{n}} = \frac{nE}{R}$. Then the third law is deduced, *that when the external resistance in comparison with the internal resistance is overlooked, the intensity of the current increases in proportion to the surface extent of the element.*

If, on the contrary, the external resistance is great in com-

parison with that of the element, the intensity of the current is not augmented by increasing the surface-extent of the element, thus: $I = \frac{E}{\frac{R}{n} + r} = \frac{E}{r}$.

Hence, when the circuit-resistances are very great it is necessary to augment the intensity of the current by proportionately increasing the number of the elements, giving a surface as small as desirable. If, however, the external resistances are very small, the intensity of the current is augmented by increasing the surface of each element, without augmenting their number.

Now, in the practical application of electricity, the external resistances by the human body are so great that the internal resistances may be neglected; hence, in electrotherapeutics the surface-extent of the elements is of no importance, the intensity of the current being determined by the number of the elements. It makes no gain if the elements are a few feet square or a few inches; their number only determines the intensity of the current.

If the galvano-cautery is used, then the external resistance is very small. Here the internal resistance is only to be considered, and you increase the surface-extent of the elements as the resistances diminish proportionately to the increase of surface-extent, and the intensity of the current increases with the increase of the surface-extent of the elements.

The *density* of an electrical current and the *intensity* of it are two totally different things. Thus, let L represent the length of the conductor and Q its transverse section, then the resistance will be represented by $\frac{L}{Q}$, that is, the resistance is proportional to the length of the conductor, and inversely proportional to the square of its diameter. If now D represent density and I the intensity of the current at the transverse section of the conductor, the formula will be $D = \frac{I}{Q}$. Hence the density of the current, the length of the

conductor remaining the same, can be varied by varying the transverse section. If two elements, as copper and zinc, are united by a nerve, the internal resistance will be extremely small in comparison with that of the nerve, and can be overlooked. If now r represent the resistance of the nerve, then $r = \frac{L}{Q}$, that is, *the resistance of a conductor is proportional to the length and inversely proportional to its section.*

Taking the law of Ohm, $I = \frac{E}{r}$, and then substituting the value of r for it, the formula will be

$$I = \frac{E}{\frac{L}{Q}} = \frac{EQ}{L}$$

Now it has been shown that the density of the current is equal to $\frac{I}{Q}$, and then replacing I by its value, the formula is

$$D = \frac{EQ}{LQ} = \frac{E}{L}.$$

If in place of the first nerve a second is placed whose section is twice the size of the former, then

$$I = \frac{E + 2Q}{L}. \qquad D = \frac{I}{2Q} = \frac{E}{L} + \frac{2Q}{2Q} = \frac{E}{L}.$$

Hence, *the density of an electrical current is not changed, although the section is double. If now the internal resistance is overlooked in comparison with the external resistance, the density of the current will not be changed by the increase of the transverse section of the conductor.*

If the external resistance is extremely small in comparison with the internal resistance, then the density of the current is inversely proportional to the transverse section. In

this case the intensity of the current always remains the same, whatever may be the section of the conductor, as the resistance is always excessively small; hence $I = \frac{E}{r}$ and $D = \frac{I}{Q}$, then $D = \frac{E}{2\,Q}$; hence the density will be as much smaller as Q is greater, Q being the transverse section.

The electric currents commonly used in practice are the induced and galvanic. Induction-machines usually have two cylinders covered with wire, the one inclosing the other. The outer cylinder is called the secondary spiral and the inside one the primary spiral, which contains inside the coil of wire a number of wires lying in a longitudinal direction. Now when the current from the cell goes through the primary spiral it produces magnetism of the wires inclosed by the primary spiral, which induces a current of electricity in the secondary coil. When the current in the primary spiral is broken, then another current is induced in the secondary spiral. The direction of the current in the secondary spiral is in an opposite direction to that in the primary spiral, but when the current is broken, then the secondary current is in the same direction as the primary current. The current generated in the primary coil has been called by Duchenne the extra-current, but Rosenthal has shown that it has no properties different from the currents of the secondary spiral.

The opening current is, physiologically speaking, much stronger than the closing induction current Duchenne believed that the extra-current acted with special force on the muscles, whilst the currents of the secondary spiral acted greater on the sensory nerves of the skin. This statement of Duchenne's is true for his apparatus, because his primary coil contains a few very thick coils, and the secondary spiral a great number of coils of very fine wire. Here the extra-current had greater intensity than the currents of the secondary coil, and consequently acted differently in a physiological sense. The extra-current and the currents of the

secondary coil are all induced currents. Induction-apparatus also contain an electro-magnet to automatically close and open the current.

The constant galvanic current consists of a number of cells united together, which give off a current which is frequently used without being broken. The direction of the current can be changed by an instrument called the *commutator.* This current is also varied in intensity by an instrument called the rheostat. A galvanometer is also used to estimate the variations of temperature or to measure the intensity of the current.

As long as the constant current remains uniform in intensity, there is neither nervous impulse nor contraction of the muscle, except in sudden changes of the intensity, as in the opening and closing of the current. The variations of the constant current only produce contractions.

Physiological Action.

On nerves, the induced currents produce a great excitation; on muscles, a prompt and permanent contraction. In induced currents the negative pole has most activity, and is the one most used to produce excitation. Although the poles are alternately negative and positive, the negative pole of the opening shock is meant, as this kind of shock is the most active, physiologically speaking. To irritate muscles they are excited directly, or the negative pole is placed on the point where the motor nerves emerge. By irritating the muscle through the nerve a less intense current is needed, and necessarily less pain is produced. The points of emergence of the motor nerves are called usually Ziemssen's. In irritating the trunk of the facial nerve the anode is placed on a point inside the concha. To excite the deltoid muscle the anode is placed just above the clavicle, towards its outer extremity. To irritate the biceps of the arm the point is between the two heads of this muscle. The median nerve is best reached at the lower third of the humerus and pressed against the bone. The ulnar nerve is best stimulated in the

groove between the olecranon and the internal condyle of the humerus. The radial nerve is reached between the insertion of the deltoid and the external condyle of the humerus.

When constant currents are applied to muscles, contractions are produced on the opening and closing of the current; the closing contraction being stronger when a constant current passes through a nerve. It is found that the region of nerve about the positive pole is decreased in excitability, the nerve here being in a state of anelectrotonus, whilst the region of nerve about the negative pole is in a state of katelectrotonus, a state of increased excitability. When the current is running towards the muscle it is called a descending current. When it is running from the muscle it is an ascending current. The contraction laws of Pflüger's are explained as follows:

The nerve is excited when the molecules pass from the ordinary state to a state of greater mobility, katelectrotonus, or when they pass from a state of less mobility, anelectrotonus, to the ordinary state. The nerve is not irritated either by its passage from the ordinary state to the state of less mobility, anelectrotonus, or by its passage from the state of greatest mobility, katelectrotonus, to the ordinary state.

The laws are as follows:

O, Opening of the current.
S, Closing of the current. R, Rest of muscle.
C, Contraction of the muscle.

Strength of current.	Ascending current.		Descending current.	
Strong.	S—R	O—C	S—C	O—R
Medium.	S—C	O—C	S—C	O—C
Feeble.	S—C	O—R	S—C	O—R

Cyon experimented upon healthy man, and found that the above laws held good. Heidenhain has also shown that a

fatigued muscle can be restored to its pristine vigor by the ascending current, which is of greatest importance. Rosenthal, on himself, has discovered that every constant current increases the irritability of the nerves for its own opening, and lowers it for the closing of the opposite current, and on the contrary lowers it for its own closing and increases it for the opening of the opposite current. This holds good also for the sensory nerves of man. In the practical application of electricity, the (1) differences of conductivities, and (2) of specific irritability of tissues must be observed. The tissues which oppose the least resistance are most affected by electricity, as it always follows the easiest path homeward. The resistance to the passage of electricity by the nerve compared with the muscle is as 1.9—2.4 : 1.

Bone conducts sixteen to twenty times worse than muscle. The resistance of the skin is equal to five thousand units of Siemen's. The back of the neck and upper segment of the spinal cord conduct better than the lumbar segment. To irritate the muscles and not the skin, strong currents are used, the skin being benumbed by ice or chloroform. When the electrodes are of various sizes, the current will be greater in the tissues about the smaller electrode. The nearer the electrodes are to each other the greater the density of the current. When two electrodes are placed on the body, the waves of electricity are directed in such a manner that the greatest density is on a straight line joining the electrodes. When it is wished to only irritate the sensory nerves of the skin, the skin about the small electrode is powdered to make it dry, whilst the large electrode is moistened. To irritate the spinal cord by galvanism is quite easy, because the spinal cord offers less resistance than the bony vertebræ, the current traversing the path of least resistance. The induced current excites the spinal centres too much and should not be applied. In galvanization of the head the direction of the current should be towards the head to diminish the circulation, and from it to increase the amount of blood. The séance with induced currents should be about five minutes,

with constant currents about fifteen minutes. The intensity of muscular contraction is in direct relation to the intensity of the electric current. If it is desired to irritate the muscles or deeper tissues, the skin is moistened with water to diminish the resistance to the penetration of electricity. When the electrodes are pressed firmly against the skin the sensibility is diminished. If the skin is to be excited a wire brush electrode may be employed instead of the small dry electrodes. Here each wire gives off electricity, and the density of the current is very great in these points. The greater the number of wires in the brush the greater the irritation. The physiological and pathological differences between the action of the induced and galvanic currents are due to differences between the duration and density of the galvanic currents compared with the to-and-fro wave of the induction-apparatus.

The constant current produces electrotonic conditions and electrolysis, whilst induction-currents either do not or in very feeble degree. The induced currents excite more than the constant currents, and hence are not applicable to the spinal cord or brain, and sometimes fail to produce muscular contraction when the galvanic current is able to. Legros and Onimus formulate the laws of constant currents as follows:

1. Descending currents act most energetically on the motor nerves. 2. Ascending currents act most on sensory nerves. 3. The excitability of nerves is diminished by a descending current and augmented by an ascending one. 4. On the spinal cord the descending current acts directly upon the motor nerves and not by reflex action. 5. The ascending current excites the irritability of the spinal cord, and acts on the motor nerves by reflex action. 6. The descending current along the spine depresses reflex action and the ascending exaggerates them.

Action in Disease.

In anæsthesia faradic currents are used; in hyperæsthesias they can also be used, but the descending constant is best.

Here the positive pole is placed on the spinal cord, where the nerves leave, and the negative below the neuralgic region. In peripheral palsy the faradic current is used, unless the muscles only contract under the influence of the constant current. The faradic current is not applied to the spinal cord; here the galvanic current is used. In infantile paralysis the muscles generally do not respond to faradic currents; here the constant current, going from the spine to the muscles, is used. In progressive muscular atrophy the constant current is passed from the spine to the affected muscles. Locally to the wasted muscles faradism may be applied. The most to be hoped for is the arrest of the disease. In chronic myelitis the ascending constant current may be used. In one case of localized myelitis, I have seen the constant current in three months restore sensibility, which, as well as motility, was absolutely lost. Motility in the course of a year also returned.

In tabes dorsalis, during the stage of irritation, weak descending currents are used. When the stage of excitation is diminished, then strong galvanic currents. In fatty muscular atrophy galvanic currents are applied to the spinal cord. In hysterical paralysis, faradism by the wire-brush to the skin, and galvanic currents flowing from the spinal cord to the muscles. In lead paralysis galvanic currents are used on the nerves, and faradic currents to the affected muscles. The alternate use of faradic and galvanic currents is better than either alone. In diphtheritic paralysis faradic and galvanic currents are used. In reflex paralysis the galvanic stream is applied to the cord, and from there to the muscles. In chorea the ascending constant current is used, and is preferred to the faradic. In writers' cramp, faradism to the muscles and galvanic currents from the spine and nerve-plexus. In facial paralysis the faradic current is used on the muscles and the negative pole of the galvanic current on the spine, and the positive pole on the motor point. Care must be taken not to injure the sight by strong constant currents. In paralysis of cerebral origin, as after apoplexy, the electric current

should not be used before two to five months have elapsed. If constant currents are used, the ascending ones are preferred. In amenorrhœa one pole of the galvanic current is placed in the middle of the lumbar region, the other on the cervix uteri, the current being broken.

All conductors become warmer by the passage of electricity, and as platinum opposes a great resistance, and is a poor conductor of both heat and electricity, it is used. The platinum wire should be thin and short. The wire is heated to a white heat, then allowed to cool and applied to the tumor or body to be removed, and then heated to its full height. Dr. Byrne, of Brooklyn, has devised a very ingenious battery for galvanocautery.

ADDENDUM.

Luchsinger discovered in the lumbar section of the spinal cord nerve-centres which preside over the secretion of sweat. He found that heating, asphyxia and nicotin excited them. Pilocarpin, also by an action on the nerve-endings in the cells of the sweat-glands, caused increased perspiration, whilst atropia prevented this action of pilocarpin, but if larger doses of the latter were given sweating ensued.

WHERE INSTRUMENTS MAY BE PROCURED.

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Page 19, second line from bottom, read "sulphide" for "chloride."

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